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RELATION OF FIELD CONTRACTION TO BLOOD PRESSURE IN CHRONIC PRIMARY GLAUCOMA

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It is common experience that in cases of chronic primary glaucoma there is often an inconsistency between the height of the intraocular pressure and the rate of contraction of the visual fields. There are those cases in which the intraocular pressure is slightly above normal, or even normal, and the fields show progressive contraction, and there are those in which the intraocular pressure is well elevated and the fields show little or no tendency toward progressive contraction. Certainly the elevated intraocular pressure is the most important factor in the contraction of a field, but there are other factors which tend in some instances to nullify and in other instances to augment its deleterious effects. If these factors could be determined and their relation be better understood, indications for treatment would be clearer and the prognosis more accurate.

If it is assumed that the field changes in glaucoma have a vascular basis, the relation between the intraocular pressure and the retinal blood pressure will appear to be an important factor in determining the rate of change in the fields. Lauber [1] reported on the importance of this relation, particularly in primary optic nerve atrophy. He stated the belief that the atrophy and the contraction of the fields result from an altered relation between the normal intraocular pressure and the subnormal retinal vascular pressure and suggested that the field changes in

From the Institute of Ophthalmology of Presbyterian Hospital and Columbia University College of Physicians and Surgeons.

Read before the Section of Ophthalmology of the New York Academy of Medicine, Feb. 16, 1942.

1. Lauber, H.: (*a*) Treatment of Atrophy of the Optic Nerve, Arch. Ophth. **16**:555-568 (Oct.) 1936; (*b*) Das Verhältniss des allgemeinen Blutdruckes und des Druckes in den Netzhautgefässen zum intraokulären Druck und sein Einfluss auf den Sehnerven und die Netzhaut, Ztschr. f. Augenh. **87**:65-76, 1935.

glaucoma are due to the same altered relation between high intraocular pressure and normal retinal vascular pressure. In both instances the nutrition of the retina would suffer because the intraocular pressure was either high, in the one, or relatively higher, in the other, than it should normally have been in relation to the retinal vascular pressure. Lauber [1] supported this contention in regard to primary optic nerve atrophy with evidence which has been corroborated by some investigators [2] and refuted by others.[3] No actual evidence bearing on this relation in glaucoma has been forthcoming.[4] In an effort to obtain some such evidence the present study was undertaken.

In an analysis of the relation of the intraocular pressure to the vascular pressure of the retina, the systolic, diastolic, venous and capillary pressures must be considered. Lauber [1] gave the normal retinal systolic pressure as 70 to 88 mm. of mercury and the diastolic as 40 to 56 mm. of mercury. If 26 mm. of mercury is considered the highest level of normal intraocular pressure, then the lowest level of the normal retinal vascular pressure is 14 mm. above the highest level of the intraocular pressure. Lauber [1] said that this is the condition necessary for normal capillary circulation in the retina. The retinal systolic and the retinal diastolic pressure as given by other observers (Sobański,[2a] Suganuma [5] and others) do not vary materially from these of Lauber. The determination of the retinal capillary pressure offers more difficulty, and the figures therefore vary more widely. Dieter [6] said that it fluctuates between 42 and 62 mm. of mercury, averaging 51.5. Lida and Adrogué [6] found it to be 40 mm. of mercury; Serr [6] and Bailliart [6] and Seidel,[6] 30; Baurmann,[6] 46; Duke-Elder,[6] 50 to 55, and Sobański,[6] 33 to 55. The retinal venous pressure [1b] has been given as follows: from the ages of 7 to 15 years, minimal 16 to 22 mm. of mercury and

2. (*a*) Sobański, J.: Der Blutkreislauf in der Netzhaut unter physiologischen Bedingungen, Arch. f. Ophth. **135**:375, 1936. (*b*) Arruga, H.: Nuevas orientaciones pathogénicas y terapéuticas en la atrofia tabética de las nervios ópticos, Arch. de oftal. hispano-am. **36**:365-373, 1936; Die Behandlung der Sehnervenatrophie, Klin. Monatsbl. f. Augenh. **97**:308-315, 1936.

3. Moore, E. M., and Woods, A. C.: The Pathology and Pathogenesis of Syphilitic Primary Optic Atrophy, Am. J. Ophth. **23**:1-40, 1940. Constantine, E.: A Study of the Interrelationship of Retinal and Systemic Arterial Pressures and Intraocular Tension in Normal and Syphilitic Patients, ibid. **3**:436-445, 1940. Ascher, K.: Zur Messung des intraokulären Blutgefässdruckes, Arch. f. Ophth. **139**:62-79, 1938.

4. J. Gallois (cited by Lauber [1a]) stated the belief that the field of vision suffers when the blood pressure of the patient with glaucoma is lowered.

5. Suganuma, S.: Studien über den Blutdruck in der Zentralarterie der Netzhaut bei gesunden Menschen und über seine Beziehung zum allgemeinen Blutdruck, Klin. Monatsbl. f. Augenh. **96**:74-84, 1936.

6. Cited by Lauber.[1b]

maximal 28 mm. of mercury; 15 to 40 years, minimal 20 and maximal 34, and over 40 years, minimal 33 and maximal 36.

For the purposes of this study the relation of the intraocular pressure and the retinal systolic and the retinal diastolic arterial pressure to the rate of contraction of the visual fields has been considered. Only the clinical data usually available for patients with glaucoma have been utilized. The systolic and the diastolic brachial pressure have been determined by the standard sphygmomanometer, and it has been assumed, on the basis of published figures to that effect,[7] that these are a true index of the systolic and the diastolic retinal pressure.

A series of 132 eyes with chronic primary glaucoma have been studied. All data were obtained prior to any operative procedure. In order to compare the fields of vision more easily and accurately with the

TABLE 1.—*Percentages of Visual Fields Retained*

Percentage of Field Retained	No. of Cases
0 - 10	29
11 - 20	16
21 - 30	12
31 - 40	11
41 - 50	11
51 - 60	5
61 - 70	9
71 - 80	15
81 - 90	16
91 - 100	8
	132

other factors, we estimated the amounts of field vision retained in percentages, with the planimeter.[8] The results are shown in table 1.

Most of the sphygmomanometer readings were taken at the time the patient was admitted to the hospital for operation on one or the other eye; attendant emotional reactions may have produced readings somewhat higher than they would have been under ordinary conditions. The intraocular pressure was measured with various types of the Schiøtz tonometer, and the recordings were usually not made at the time of the patient's admission to the hospital. In the large majority of instances a number of blood pressure and tonometer readings were available and their means taken for the purposes of this study.

7. Lauber,[1b] Sobański,[2a] Suganuma.[5]

8. The planimeter is an instrument used principally by engineers for computing the area of odd-shaped flat surfaces. The arm of the instrument is guided around the outline of the surface to be measured, and then the actual area is determined from a scale. We have found it satisfactory for measuring the area of charted fields of vision of any size or shape. From the actual area of field of vision retained we have calculated the percentage of field of vision retained.

To facilitate comparison, moreover, the relation of the systolic and the diastolic pressure to the intraocular pressure has been expressed in the form of a coefficient derived from dividing the former by the latter. If the mean systolic pressure were 120 mm. of mercury and the mean intraocular pressure 30 mm. of mercury, the coefficient would be 4. Thus in each of the 132 cases of chronic primary glaucoma we had the percentage of visual field retained, the systolic coefficient (mean systolic blood pressure divided by mean tension) and the diastolic coefficient (mean diastolic blood pressure divided by mean tension).

In order to determine whether the rate of field contraction depends not on the height of the intraocular pressure but rather on the relation between it and the arterial pressure, an effort was made to establish a relatively normal ratio between the systolic or the diastolic pressure and the intraocular pressure, as expressed in a coefficient. Any deviation from that normal might then be expected to be reflected in a contraction of the field. For instance, if the normal systolic pressure is taken as 125 mm. of mercury and the normal intraocular pressure as 25 mm. of mercury, then the normal coefficient will be 5. If the systolic pressure were 125 mm. of mercury and the intraocular pressure 50 mm. of mercury, then the coefficient would be 2.5. This would be below normal, and the field would be expected to show a greater tendency toward contraction. If the systolic pressure were 250 mm. of mercury and the intraocular pressure 50 mm. of mercury, then the coefficient would be 5, which is normal, and little or no tendency toward field contraction would be expected. If the systolic pressure were 75 mm. of mercury and the intraocular pressure 25 mm. of mercury, then the coefficient would be 3 and thus abnormal. The existence of such a relation would explain the cases of high intraocular pressure and little or no field changes and the cases of normal intraocular pressure and definite field changes. The results of these comparisons would also reveal which coefficient, the diastolic or the systolic, would be the more reliable indicator of field contraction.

The results in our series of 132 cases are shown in table 2.

Eyes with the percentage of field retained ranging from 100 to 70 (38 eyes) had a mean systolic coefficient of 5.65 and a mean diastolic coefficient of 3.21. Eyes with the percentage of field retained ranging from 70 to 35 (31 eyes) had a mean systolic coefficient of 4.61 and a mean diastolic coefficient of 2.28. Eyes with the percentage of field retained ranging from 35 to 0 (62 eyes) had a mean systolic coefficient of 4.05 and a mean diastolic coefficient of 2.33. Eyes with the percentage of field retained ranging from 100 to 50 (52 eyes) had a mean systolic coefficient of 5.65 and a mean diastolic coefficient of 3.19. Eyes with the percentage of field retained ranging from 50 to 0 (79 eyes) had a mean systolic coefficient of 4.0 and a diastolic coefficient of 2.28.

TABLE 2.—*Percentage of Field Retained, Systolic Coefficient and Diastolic Coefficient in 132 Cases*

Percentage of Field Retained	Systolic Coefficient	Diastolic Coefficient	Percentage of Field Retained	Systolic Coefficient	Diastolic Coefficient
100	6.60	4.44	38	4.06	2.03
100	4.64	3.71	38	4.41	2.22
100	5.33	2.53	37	2.65	1.62
100	5.0	2.37	35	4.72	2.77
96	4.32	2.90	35	6.07	3.07
95	5.55	3.51	35	5.33	3.66
91	6.0	4.0	35	6.4	3.42
90	3.38	2.10	33	5.72	3.10
89	4.80	3.20	33	5.4	2.9
88	3.66	1.66	28	3.41	1.70
87	9.25	5.0	28	5.31	2.87
87	5.42	2.57	27	7.82	3.91
84	4.51	2.74	27	3.48	2.20
84	5.0	2.53	25	3.34	2.83
84	10.7	5.0	24	3.57	2.17
84	2.65	1.62	23	4.83	3.06
83	8.63	4.09	23	5.76	3.65
83	9.71	4.76	22	5.9	3.1
83	3.20	2.10	21	3.38	2.0
81	4.50	2.83	20	3.60	2.17
80	6.78	3.21	20	4.16	2.72
80	5.0	3.27	18	3.0	1.61
80	5.12	3.37	17	1.80	1.04
80	2.93	1.60	17	4.93	2.4
79	4.70	2.59	16	4.04	2.14
79	8.63	4.09	15	3.71	1.85
78	4.68	2.59	14	2.38	2.28
78	8.25	4.80	14	3.33	2.22
76	8.85	3.94	14	4.37	2.08
76	5.0	3.18	13	5.14	3.02
76	2.32	1.60	12	5.80	3.22
76	2.79	1.87	11	3.18	1.72
75	5.62	3.33	10	3.69	1.95
75	4.70	2.59	10	2.58	1.34
74	8.2	4.80	10	2.31	1.2
72	7.11	5.46	10	4.25	2.85
71	5.76	2.92	8	2.50	1.16
71	5.66	3.33	6	5.62	2.81
70	4.21	2.42	6	3.51	2.22
69	6.81	4.00	5	6.0	3.33
68	3.66	2.32	4	5.23	2.56
68	6.07	3.57	3	5.36	2.88
67	4.48	2.24	2	3.61	1.95
64	7.29	3.29	2	2.70	1.87
63	4.50	3.09	2	2.58	1.45
63	4.03	1.73	2	3.62	2.5
60	6.96	5.07	2	4.90	2.54
60	5.0	2.76	2	3.54	2.28
57	7.60	4.17	2	4.54	2.03
55	7.82	4.60	1	4.64	2.5
55	4.10	2.05	1	4.47	2.63
52	5.65	2.55	1	2.50	1.42
50	3.24	2.32	1	2.07	1.2
47	2.23	1.34	1	4.35	2.11
46	3.12	1.83	1	3.33	1.66
45	4.66	2.22	1	3.51	2.0
45	4.24	2.27	0.8	2.66	1.33
44	5.50	2.92	0	4.21	2.42
44	4.64	2.85	0	4.08	2.35
44	2.30	1.57	0	2.0	1.53
44	3.60	1.82	0	3.40	1.82
44	6.28	3.42	0	3.20	1.74
44	3.76	2.28	0	4.38	2.22
43	3.66	2.32	0	4.1	3.6
38	3.68	1.97	0	2.05	1.11
38	3.0	1.89			

From these figures it may be deduced that a systolic coefficient of from 5.75 to 6.0 or higher and a diastolic coefficient of from 3.25 to 3.50 or higher may be considered normal. This does not mean, however, that a patient with coefficients in these normal ranges or higher might not show contraction of the visual fields, or vice versa, for the coefficients were not always consistent. All that can be said is that coefficients within these specified normal ranges, or higher, indicate that the retention of fields will tend to be protracted, while coefficients lower than these norms indicate that the loss of fields will tend to be rapid. The systolic and the diastolic coefficient appeared to be of equal significance.

Among the sources of error inherent in the procedure followed in making determinations, the more obvious were the following:

1. It was impossible to determine the exact duration of the glaucoma. This is an important factor, since an eye with a coefficient slightly below normal but with glaucoma of long duration may have shown the same percentage of field retained as one with a low coefficient and glaucoma of short duration.

2. The great variability of the blood pressure and the intraocular pressure may have led to incorrect determinations.

3. It was impossible to determine the extent to which miotics had been used in the past. This factor is important in relation to the readings of the intraocular pressure. For example an eye may have had to tolerate a mean intraocular pressure of from 30 to 35 mm. of mercury for months or years before observation but after the use of miotics have had one that ranged between 20 and 25 mm. of mercury. Before this eye was observed, therefore, the coefficient may have been lower than normal, but in our figures it would be represented as normal.

4. The degree of sclerosis of the retinal vessels could have influenced our findings. Vessels with sclerosis could have better resisted the intraocular pressure.

In view of these sources of error it is clear that the coefficients as determined in this study cannot be accepted unconditionally and that the results merely indicate a trend toward a relation between the intraocular pressure, the blood pressure and the contraction of the visual fields.

OBSTACLE TO SQUINT TRAINING—AMBLYOPIA

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Amblyopia is one of the four major obstacles [1] in the treatment of squint. It may be found independent of squint, but when it is associated with squint one does not know whether it is the cause or the result of the strabismus.

Wolff [2] has stated that in amblyopia of the toxic type the poison may act on either the nerves or the muscles, affecting the action of the retina, the optic nerve, the ciliary muscle (accommodation) or the sphincter pupillae. In a case of toxic amblyopia, by a careful examination, the purpose of which is to find the exciting cause of the condition, and by continuous observation of the pathologic area involved, one can arrive at a fairly definite conclusion with respect to the ultimate prognosis. This is not true, however, with regard to either the congenital or the acquired type of the so-called entity amblyopia exanopsia, the visual defect without any demonstrable signs or ophthalmoscopic changes. Many of the tests used in the diagnosis of this condition are subjective, the results depending on the veracity and intelligence of the patient and on the psychologic effect which each test has on him. In the patient with associated squint, the results of the objective tests also may vary according to the cause of the strabismus.

One can therefore understand how questionable results have been obtained in amblyopia, since even the original vision, as will be shown, is not definitely established by a single examination.

In an attempt to arrive at some conclusion in the study of this interesting problem of visual acuity, we have studied 68 patients during a period of several months.

These patients were unselected. They were divided into four groups: (1) children with amblyopia and squint, (2) children with amblyopia

From the Squint Clinic of St. Christopher's Hospital for Children.

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1. Feldman, J. B.: Clinical Observations on the Treatment of Squint, Arch. Ophth. **26**:38 (July) 1941.

2. Wolff, E.: A Pathology of the Eye, Philadelphia, P. Blakiston's Son & Co., 1935.

without squint, (3) adults with amblyopia and (4) a miscellaneous group including patients with normal eyes and those who had had amblyopia and whose vision improved to 5/5 with glasses. Fifty per cent of the patients were children treated for amblyopia or squint in the orthoptic clinic; the balance were adults from private practice and children who came to the ophthalmic clinic for refraction.

Routine studies were done as follows:

A. Each patient had his vision tested with and without glasses on a number of charts. Further to insure comparable results, all tests of of his visual acuity were made at the same sitting.

B. The patient was then examined ophthalmoscopically.

C. After the history had been recorded, the field was taken with a tangent screen. In some instances several patients were in the room at one time so that we might note the psychologic effect. When the patient was comparatively intelligent and had fusion, a stereoscopic tangent screen was used. When excellent cooperation was obtained, a field was taken with the perimeter.

D. The grade of binocular vision was obtained with the synoptophore.

E. Finally, the angle of squint was taken both with the perimeter and with the synoptophore.

AMBLYOPIA

Amblyopia is a localized area of blindness in the central field of vision, usually of one eye, without any retinal disturbance to account for it. In many patients with squint, possibly through continuous suppression of vision, the obstacle amblyopia develops, and in these patients it is recognized early.

However, there are patients who are definitely amblyopic without any history of squint, and some, since they see well with the unaffected eye, have the entity for many years without its being recognized. Others have known of their shortcoming but "never did anything about it."

HEREDITY AND SEX

It is interesting that among the children examined there were 6 whose immediate relatives definitely had an amblyopic eye. The relatives of 2, in addition to their amblyopia, had squint. The presence of squint was observed in the immediate families of 13 of our patients with amblyopia.

Half of our entire group of patients with amblyopia were male and half female.

REFRACTION

A high refractive error was commonly seen in the members of the family of the patients with amblyopia. It was noted, however, that in

the amblyopic patient the comparatively higher refractive error did not necessarily affect the prognosis; some patients with high amblyopia and a high refractive error improved sooner than the patients with low grade amblyopia and a simple error.

No predilection was shown for a particular eye so far as the amblyopia was concerned, there being about as many right as left eyes afflicted. There were almost as many hyperopes (in many of whom the error was high) as anisometropes, with proportionately fewer patients with hyperopic astigmatism. The proportion of myopes was the least.

Vogt [3] claimed that ametropia is not a definite causative factor in amblyopia. This was demonstrated by our patients, about 18 per cent of whom had a refractive error of less than 3 D. One half of 1 per cent were emmetropic. This figure is somewhat less than that quoted by Grandi [4] (2.5 per cent).

VISION

Naturally the diagnosis of amblyopia is based on the existing vision, and a vision of less than 6/15 is considered evidence of an amblyopic condition provided there are no ophthalmologic or other findings to account for it. When the vision improves rapidly in a case in which a diagnosis of amblyopia has been made, the question sometimes arises as to whether the vision as originally given was correct. To determine how great the discrepancy was for our patients, we decided to test the vision of each patient with three different kinds of visual acuity chart. The number type of Snellen chart was chosen, the purpose being to select a chart which could be read by all adults and by children. Some adults could not read English. The same type of chart (Keystone number card) was used in the telebinocular. To insure that all examinations would be done under like conditions, since some of our older patients were presbyopic, only the first test was done with and without glasses on the Snellen number chart. All succeeding visual tests of patients young and old were done with glasses on, both with the telebinocular number chart and with the illiterate chart (Reber).

Finally the vision of each eye separately was tested on the Snellen number chart with the glasses worn and augmented by a field glass so that we might note whether the vision was improved still further. The use of this glass we felt would assist us in ruling out those patients who were beyond improvement. For this type of study a telescopic spectacle (Wollensak-Allscope) with 3¼ magnification was used. Higher magnification did not prove more valuable.

3. Vogt, A.: Klin. Monatsbl. f. Augenh. **103**:291, 1939.

4. Grandi, G.: Boll. d'ocul. **14**:1479, 1935.

No.	Name	Age	Sex	Refraction *	Duration, Years	Vision †								
						Snellen Chart Without Glasses		With Glasses at 5 Meters						
								Snellen Chart		Illiterate Chart		Telebinocular		With Magnifier
						Right	Left	Right	Left	Right	Left	Right	Left	Right
1	M. B.	11	♀	H	8½	24	6	6	6	30	6-3	30	7.5	15
2	T. B.	8	♂	A	6	60	9	60	6	60	6	70	5	60
3	H. B.	9	♂	A	6	12	6	12	6	12	6	15	12	6
4	P. C.	10	♂	H	8½	6	30	6	30	6	30	5	70	5
5	J. D.	6	♂	H	½	12	12	12	12	12	12	25	25	9
6	E. D.	12	♂	HA	4	15	12	15	9	24	15	15	5	6
7	L. E.	8	♀	H	4	30	8	30	8	30	8	30	14	10
8	M. G.	14	♀	H	10	30	5	24	5	24	5	25	5	15
9	H. G.	11	♂	M	1½	15	30	24	30	60	60	20	25	5
10	W. G.	11	♂	HA	5	30	6	30	6	30	6	70	5	30
11	D. H.	12	♀	A	7	6	15	6	15	6	24-2	7.5	30	4
12	W. K.	10	♂	A	12	1/60	6	60	5	60	5	60	5	30
13	C. K.	9	♂	A	8½	15	24	12	15	12	12	10	10	9
14	P. K.	8	♀	A	5	15	60	9	30	6	35	8	70	—
15	B. L.	12	♂	A	8	5	24	5	24	6	30	5	20	4
16	T. M.	7	♂	A	5	70	9	60	9	60	6	70	5	30
17	J. P.	10	♀	HA	7	30	15	30	12	24	6-2	15	5-1	6
18	E. R.	11	♂	A	3	12	15	9	12	12	60	10	40	6
19	R. S.	10½	♂	A	7½	6	24	5	24	5	24	5	10	5
20	R. S.	8	♂	HA	4	12	15	9	15	9	15	10	40	6
21	K. T.	12	♀	H	8	1.5/60	6	2.5/60	5	1/60	5-2	—	8½	60
22	D. T.	7	♀	H	4	9-2	21.3	9	21.3	6	21.3	15	20	9
23	I. W.	8½	♀	H	5	24	12	24	15	24	15	40	15	6
24	H. W.	12	♂	A	6	24	6	15	5	24	5-2	25	5	12
25	D. Z.	8	♀	HA	4½	24	12	15	12	30	15	20	8	12
26	G. Z.	13	♂	H	9	12	6	12	6	12	5-2	15	5	6

* H indicates hyperopia; A, anisometropia; HA, hyperopic astigmatism; M, myopia, and MA, myopic astigmatism.

† The number type of Snellen chart and illiterate chart (Reber) was used, and a number chart was used with magnifier. The tests in which glasses were used were comparable with telebinocular examination of presbyopes with amblyopia. Since vision was tested at 5 meters, the values should be combined with 5. That is, 24 and 6, for example, indicate vision of 5/24 in the right eye and 5/6 in the left.

‡ A 4.4/1,000 stimulus with 7 foot candles of illumination was used in the tangent screen test, and a 1/200 stimulus with 3 foot candles of illumination in the perimetric test.

§ In some cases the visual acuity was tested before refraction was attempted.

Fields ‡			Angle of Squint		Grade of Binocular Vision			
Tangent Screen				Synopto-phore, Prism Diopters	Simultaneous Macular Perception			
Monocular	Binocular	Perimeter	Perimeter, Degrees			Fusion	Stereopsis	Comment
1: normal 1: both eyes, without Mariotte blindspot	..	..	30	20	..	+	?	Operated on at 5 yr.; convergent squint corrected; mother, amblyopia in left eye; father, cross eyed
1: contracted 1: normal	..	..	32	50	—	..	..	Operated on at 5½ yr.; squint unimproved; false macula; brother, squint
both eyes, without Mariotte blindspot	..	1: both eyes contracted	40	40	..	Temporary	..	20 degree convergent squint; father, squint; uncle born blind; original vision 6/30; false projection improved; suppression, left eye
both eyes, normal	..	..	10	20	..	+	..	35 degree convergent squint; operated on and improved cosmetically; false projection; left eye, fixation weak
both eyes, contracted	..	..	10	28	..	..	+	Vision 2 mo. before, 6/22; father, constant squint; parallelism with glasses
both eyes, without Mariotte blindspot	..	..	Ortho	Ortho	..	+	..	Squint improved
both eyes, normal	..	..	Ortho	5	..	+	..	Occasional squint; mother, convergent squint
both eyes, normal	..	..	20	26	+	..	..	Uncle and aunt, squint; squint developed in patient after auto accident; right hyperphoria of 6 P. D.; operation; false projection
both eyes, without Mariotte blindspot	..	..	10	6	..	+	..	Family history irrelevant; visual acuity taken § before refraction was done
both eyes, normal	..	..	Ortho	Ortho	+	..	..	Strong suppression, right eye, not overcome by 1 yr. of orthoptic training; eyes parallel; brother, squint
both eyes, normal	..	..	12	10	..	+	..	Operation for squint 2 yr. before; eyes parallel; false projection occasionally seen
both eyes, normal	..	..	10	12	..	+	?	Squint training for 1½ yr.; no operation; mother, squint and amblyopia; suppression, left eye
both eyes, without Mariotte blindspot	..	..	Unsatisfactory	15	..	+	..	Squint improved with 1 yr. of orthoptic training, but no change in visual acuity
both eyes, without Mariotte blindspot	..	..	5	8	..	+	?	Father, amblyopia in left eye; patient, convergent squint, left eye; eyes parallel with 2 yr. orthoptic treatment; hyperphoria of 4 P. D.; false projection improved
both eyes, normal	..	..	10	25	..	+	?	Operation at 10 yr.; false projection treated, with good but not permanent cure; father, high refractive error
right eye, without Mariotte blindspot; left eye, normal	..	..	10	20	+	?	..	Right eye, marked suppression; orthoptic treatment for 6 mo.
1: both eyes, without Mariotte blindspot 1: normal	1: both eyes, full	..	Ortho	5	..	..	+	Strong partial suppression, right eye; occasional squint
both eyes, normal	..	..	10	10	..	..	+	Squint improved with 1½ yr. treatment but no change in vision
both eyes, without Mariotte blindspot	..	..	Ortho	10	+	..	..	No orthoptic training; eyes parallel; strong suppression, left eye
both eyes, without Mariotte blindspot	..	1: both eyes, contracted	10	10	..	+	..	Original vision 15/50 and 13/200; orthoptic training 2½ yr.
both eyes, without Mariotte blindspot	..	..	20	20	+	..	..	No one in family except patient has squint
both eyes, full; left eye large Mariotte blindspot								
both eyes, without Mariotte blindspot	..	..	10	25	+	Unsteady	..	Uncle, squint; patient operated on 1 yr. before; had vision of 18/40 and 18/200; questionable fixation; false projection improved
1: both eyes, normal 1: both eyes, without Mariotte blindspot	..	..	8	10	..	+	..	Convergent squint, 45 degrees; operated on 1 yr. before; had vision of 6/60 and 6/24; orthoptic training for 1½ yr.
1: both eyes, without Mariotte blindspot 1: right eye, without Mariotte blindspot	1: both eyes, full	1: both eyes, slightly contracted	15	Ortho	..	+	?	2 uncles and a sister, squint; patient's eyes in good position
both eyes, without Mariotte blindspot	..	..	10	15	+	?	..	Brother and aunt, squint; alternating convergent squint, 25 degrees; strong alternating suppression; fusion obtained with stimulation
both eyes, normal	..	..	Ortho	5	..	..	+	Orthoptic treatment for 2 yr.; false projection improved; patient discharged

ACUITY TESTS

In reviewing the results of the visual acuity tests, we observed that for only 41 per cent of the patients with amblyopia did the values from two or more of the tests coincide (tables 1, 2, 3 and 4).

TABLE 2.—*Data on Children with Amblyopia but*

						Vision									
								With Glasses at 5 Meters							
						Snellen Chart Without Glasses		Snellen Chart		Illiterate Chart		Telebinocular		With Magnification	
No.	Name	Age	Sex	Refraction	Duration, Years	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
27	L. A.	11	♂	MA	5	60	60	15	24	30	30	10	15	9	12
28	E. C.	12	♂	H	8	5	21	5	15	6	60	5	20	5	12
29	G. C.	8	♂	A	1	24	24	24	24	30	30	10	15	15	15
30	R. C.	9	♂	HA	3	30	30	15	15	24	24	15	15	12	9
31†	D. G.	12	♂	H	6	12	9	12	9	12	9	10	5	9	6
32	E. G.	8	♀	A	¼	9	24	9	12	6	15	5	5	5	60
33	P. G.	11	♀	M	2	24-1	30	12	15	15-2	24	20	20	6	6
34	S. H.	9½	♂	A	⅛	24	6	24	6	30	5	25	5	6	5
35	A. K.	10	♀	MA	1½	30	30	15	15	24	24	15	20	6	6
36	R. K.	10	♀	A	⅛	30	30	15	24	24	24	25	25	6	6
37	M. L.	9	♂	HA	2	60	24	15-2	15	24	24	25	25	9	9
38	N. L.	10	♀	A	1	30	9	2.5/60	9	2/60	25	50	8	15	9
39	S. S.	9	♂	A	2	6	30	6	24	6-2	30	5	8	4	6
40	M. T.	9	♀	A	⅓	60	15	30	12	30-1	9-2	25	6	9	9
41	F. W.	12	♂	A	½	22	5	15	5	22	5	10	5	12	6
42	H. W.	12	♂	A	4	2/60	4/60	24	15	60	15	60	60	12	12

* This table contains data on patients with amblyopia and "apparent" ocular parallelism. Note that stereopsis was more frequently obtained in children with amblyopia and squint. Suppression was frequent.

Ordinarily we found use of the telebinocular to be the most discriminatory of our visual acuity tests; i. e., the values obtained by this method were more subnormal than those obtained by the other tests. Nevertheless, for 29 per cent of the patients a higher value for visual acuity was obtained with the telebinocular than with our established standard, the Snellen chart. The number of patients who showed poorer visual acuity with the illiterate chart than with the Snellen chart and the number who showed poorer visual acuity with the telebinocular than with the Snellen chart were almost equal. Almost equal values for visual

acuity were noted twice as often with the illiterate chart and the Snellen chart as with the telebinocular and the Snellen chart.

It was noted that when there was no improvement in vision with the telescopic lens the amblyopia never responded to treatment. When the

but Without Squint (Group 2) *

Fields			Angle of Squint		Grade of Binocular Vision			
Tangent Screen				Synopto-phore, Prism Diopters	Simultaneous Macular Perception	Fusion	Stereopsis	Comment
Monocular	Binocular	Perimeter	Perimeter, Degrees					
both eyes, without Mariotte blindspot	..	..	Ortho	5	..	..	+	Father, high refractive error
right eye without Mariotte blindspot; left eye, normal	..	..	5	Ortho	..	..	+	Good amplitude
both eyes, without Mariotte blindspot	..	..	Ortho	Ortho	..	+	..	Mother and aunt, high refractive error
both eyes, without Mariotte blindspot	..	..	10	Ortho	..	+	..	Right hyperphoria, 3 P. D.
both eyes, normal	1: both eyes normal; right eye, larger Mariotte blindspot	..	Ortho	12	..	..	+	Father, high refractive error; temporary suppression (graying and loss of picture)
1: both eyes, without Mariotte blindspot 2: both eyes, normal	1: both eyes, normal	1: both eyes, normal	Ortho	Ortho	..	+	?	Family history irrelevant
1: right eye, without Mariotte blindspot 2: both eyes, normal	..	..	10	Ortho	..	..	+	Eyes in good position; glasses worn by every one in family
right eye, without Mariotte blindspot; left eye, normal	..	..	Ortho	Ortho	+	?	..	Eyes in good position; strong suppression, right eye; fusion obtained but temporary
both eyes, without Mariotte blindspot	..	..	Ortho	2	..	+	?	Family history irrelevant
both eyes, without Mariotte blindspot	..	..	10	Ortho	..	..	+	Good amplitude
1: both eyes, contracted 2: both eyes, without Mariotte blindspot	..	..	Ortho	Ortho	..	..	+	Glasses prevalent in family
normal	1: normal	1: normal	10	18	+	?	..	Fixation questionable; temporary fusion; suppression shown by 2 Haitz chart examinations
both eyes, without Mariotte blindspot	1: both eyes, without Mariotte blindspot	..	Ortho	Ortho	..	..	+	Family history irrelevant
both eyes, without Mariotte blindspot	..	..	10	5	..	..	+	Snellen chart, "peppery"
both eyes, normal	..	..	Ortho	Ortho	..	..	+	Family history irrelevant
both eyes, normal	..	..	12	22	..	+	..	Family history irrelevant; no vergence; some depth perception

* Original vision of 5/15 is considered amblyopic. This type of case is included in our groups because absolute cure had not yet been obtained.

vision was not better than 6/15 with the telescopic lens strong suppression complicated the amblyopia. If the visual acuity was brought up to normal with this lens the patient, in spite of the amblyopia, usually obtained fusion with depth perception.

Two cases are worthy of mention here. As has been previously stated, the telebinocular test was the most discriminatory test we used. Nevertheless, patient G. C. (case 29, table 2) showed, in the right eye, vision of 5/10 with the telebinocular and vision of 5/15 with the Wollensak-Allscope spectacle. Patient E. G. (case 32, table 2) showed,

in the left eye, vision of 5/5 with the telebinocular and vision of 5/6 — 3 with the Wollensak-Allscope spectacle. These variations were possibly explained by inattention on the part of the patients.

The fact that the patients had their visual acuity improved to a greater or less degree by magnification (Wollensak-Allscope spectacle)

TABLE 3.—*Adults with amblyopia (G*

						Vision									
								With Glasses at 5 Meters							
						Snellen Chart Without Glasses		Snellen Chart		Illiterate Chart		Telebinocular		With Magnification	
No.	Name	Age	Sex	Refraction	Duration, Years	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
43	J. B.	58	♂	H	30	12	12	12	12	24	15	10	7.5	9	9
44	K. C.	31	♀	HA	15	30	6	15	6	24	6	7.5	5	9	14
45	H. E.	21	♀	H	15	HM	5	HM	5	HM	5	HM	5	—	—
46	H. G.	58	♂	A	15	8	60	6	30	6	20	5	15	4	12
47	M. G.	40	♀	A	25	60	9	60	6	60	5	30	5	—	—
48	T. L.	30	♀	A	10	2/60	6	2/60	6	2/60	6	—	6	2/60	9
49	H. N.	55	♂	HA	43	24	60	9	24	9	24	9	40	3	11
50	R. O.	24	♀	HA	21	2/60	24	60	6	60	6	4/60	5	30	1
51	H. P.	55	♂	A	25	6	1/60	6	1/60	6	—	6	—	5	60
52	R. P.	32	♀	A	15	6	15	6	12	6	12	5	10	5	9
53	V. R.	27	♀	A	10	7.5	2/60	5	4/60	5	4/60	5	—	5	11
54	R. S.	55	♀	HA	35	1.5/60	30	60	5	60	5	50	5	30	4
55	M. S.	23	♂	A	19	30	15	24	5	24	5	25	5	15	4

* In this group suppression was commonly seen, as was lack of vergence. Patient V. R. (case 53) and patient R. S. (case 54) claimed that their original squint had been reduced spontaneously with time. Only 1 patient obtained stereopsis, and only 1 patient (patient H. E., case 45) had proved congenital squint.

is presumptive evidence that amblyopia is a functional rather than an organic condition.

The results we obtained by checking the visual acuity with different Snellen charts are interesting. They can be explained in one way; namely, one grasps quickly that type of test chart which interests one the most. Wadsworth [5] called attention to the values for visual acuity obtained during poor and during better health.

As a control to the values obtained for patients with amblyopia, we tested a number of nonamblyopic patients with the Snellen letter

5. Wadsworth, G. F.: Boston M. & S. J. **116**:49, 1887.

chart and the Bishop-Harman illiterate chart, together with the letter card in conjunction with the telebinocular. The results were practically the same as those obtained with the amblyopic patients with the number chart. From this fact one would be led to believe that the value of such an excellent screening examination as the mass vision test [6] might be

*lyopia (Group)**

Fields			Angle of Squint		Grade of Binocular Vision			
Tangent Screen				Synopto-phore,	Simul-taneous Macular			
Monocular	Binocular	Perimeter	Perimeter, Degrees	Prism Diopters	Perception	Fusion	Stereopsis	Comment
...h eyes, normal	..	..	20	10	..	+	?	Spotty vision and sometimes attacks of sudden blindness; no vergence; questionable depth perception
...h eyes, normal	..	..	20	Ortho	+	..	..	No vergence; right eye, suppression too strong for fusion to be obtained
...t eye, normal; ...t eye, large central scotoma up to ... degrees, including ...riotte blindspot	..	3: right eye, central scotoma to and including Mariotte blindspot	30	40	—	—	—	Complete suppression, right eye; fields taken from center out and reverse; no simultaneous macular perception
...h eyes, normal	..	..	Ortho	12	+	..	..	Alternating suppression, stronger in left eye
...t eye, enlarged ...riotte blindspot	..	..	20	20	+	..	..	No vergence; 2 P. D. of right hyperphoria; right eye, suppression; sister, amblyopia
...t eye, without ...riotte blindspot	..	..	Ortho	20	?	..	..	3 brothers and 2 sisters, amblyopia with squint; patient, 10 degree convergent squint; poor fixation
...h eyes, normal	..	..	Ortho	10	..	+	..	Constantly missed middle number in telebinocular
...both eyes, without ...riotte blindspot	..	..	20	22	—	—	—	Complete suppression; right eye
...both eyes, normal ...absolute central scotoma to 10 ...grees in left eye	..	..	10	Ortho	—	—	—	Says eyes always straight; older sister, squint; complete suppression, left eye
...h eyes, normal	..	..	Ortho	2	..	..	+	Glasses worn for squint; left eye, vision spotty with magnification; paternal aunt, squint
...h eyes, normal	1: both eyes, normal	1: both eyes, normal	Ortho	Ortho	?	—	—	Family history irrelevant and no history of squint
...h eyes, normal	..	..	Ortho	Ortho	+	..	..	Complete suppression, right eye, with fusion slides
...h eyes, normal; ...er Mariotte ...dspot in right eye	..	..	20	Ortho	+	..	..	Squint; no operation; strong suppression, right eye; low grade fusion

enhanced by use of several different visual acuity charts at the same sitting for each patient studied.

FIELD OF VISION

It is conceded by a number of authors, among whom are Worth,[7] Werner [8] and Wilkinson,[9] that in amblyopia one commonly finds the

6. Sloane, A. E.: Massachusetts Vision Test: Improved Method of Testing Eyes of School Children, Arch. Ophth. **24**:924 (Nov.) 1940.

7. Worth, C.: Squint, ed. 6, Philadelphia, P. Blakiston's Son & Co., 1929.

(Footnotes continued on next page)

peripheral field and the color vision normal. Some observers have consistently found central and other scotomas. The methods by which the perimetric studies were made varied. Evans,[10] for example, used a stereocampimeter, with 15 foot candle illumination. Peter [11] advocated the short radius perimeter and found a 3 degree relative scotoma as

TABLE 4.—*Data on Ma... Group*

						Vision									
						Snellen Chart Without Glasses		With Glasses at 5 Meters							Tang
								Snellen Chart		Illiterate Chart		Telebinocular		With Magnification	
No.	Name	Age	Sex	Refraction	Duration, Years	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
56	J. B.	10½	♂	H	4	6	9	6	9	5	9	5	15	5	9
57	L. B.	13	♂	A	3	6	15	6	9	9	12	5	5	6	9
58	V. G.	8	♀	H	1	6	9	6	9	9	9	9	9	6	9
59	J. F.	12	♂	M	½	30	30	9-3	9	12-1	12	25	25	5	9
60	A. L.	12	♂	A	5	9	12	6	6	..	..	..	..	..	..
61	C. M.	8	♂	HA	3	12	12	9	9	9	6	10	10	6	9
62	N. O.	9½	♀	H	4	6	12	6	9	6	12	5	10	6	9
63	J. P.	10	♀	M	1	24	15	9	9	12	12	7	7.5	6	5
64	J. P.	9	♀	M	6	30	60	9-3	9-1	9	9	5	10	6	6
65	R. R.	11	♀	MA	1/6	24	24	6	6	6	5.2	5	5	4	4
66	N. S.	10	♀	M	¼	24	24	9	9	12	12	20	15	6	6
67	M. S.	10	♀	H	4	9	5-3	12	5.3	4	5-3	9	6	5	4
68	W. W.	10½	♂	M	⅛	30	24	6	6	9	9	7.5	5	4	5

* The difference in the values for visual acuity obtained for the same patient with different test charts is apparent in this ... in the other tables. In cases 60 and 67 the vision regressed after a vacation from training; this shows that patients with ... opia must return frequently for a recheck.

against the 2 degree positive scotoma observed by Evans. Peter in addition found an enlarged Mariotte blindspot and moderate contraction

8. Werner, L., in Swanzy, H. R.: Handbook of the Diseases of the Eye, ed. 12, Philadelphia, P. Blakiston's Son & Co., 1919.

9. Wilkinson, O.: Strabismus: Its Etiology and Treatment, St. Louis, C. V. Mosby Company, 1927.

10. Evans, J. N.: Am. J. Ophth. **12**:194, 1929.

11. Peter, L. C.: Am. J. Ophth. **15**:493, 1932.

of the peripheral field for form and for color. Travers [12] stated the belief that the scotoma of Evans was a suppression scotoma, in that both eyes were used during the test, and that the scotoma was transitory or functional in nature. By the use of a tangent screen for fixation, with another to the side, and a mirror arrangement, Travers was able to

*...s Group (Group 4)**

Fields			Angle of Squint		Grade of Binocular Vision			
Tangent Screen								
Monocular	Binocular	Perimeter	Perimeter, Degrees	Synoptophore, Prism Diopters	Simultaneous Macular Perception	Fusion	Stereopsis	Comment
...th eyes, without ...ariotte blindspot	..	..	40	90	..	+	..	Alternating squint, 45 degrees; alternating suppression; sister, squint; operation 9 yr. before, unsuccessful
...oth eyes, normal	..	..	10	Ortho	..	+	..	Original vision 20/70 and 20/50; amblyopic training 4 mo.; improvement maintained
...oth eyes, without ...ariotte blindspot	..	..	Ortho	Ortho	..	+	..	Original vision 20/70 and 20/200 2 mo. before
...oth eyes, normal	1: both eyes, normal	..	5	20	..	..	+	No vergence
...: both eyes, nor-...al ...: both eyes without ...ariotte blindspot	2: 1: both eyes, normal 1: both eyes, without Mariotte blindspot	..	15	5	..	..	+	Squint improved, as did vision; patient did not return to complete visual studies
...th eyes, without ...ariotte blindspot	..	..	Ortho-	5	..	..	+	Amblyopia with improvement of vision
...right eye, without ...ariotte blindspot ...left eye, without ...ariotte blindspot	..	..	10	5	..	+	..	Original vision 20/30 and 20/100; regression followed every improvement in vision; when treatment was discontinued; now, however, vision stays improved
...both eyes, normal ...both eyes, without ...ariotte blindspot	1: both eyes, without Mariotte blindspot	..	5	15	..	+	..	Right eye, amblyopic, improved to normal
...th eyes, without ...ariotte blindspot	..	..	Ortho	Ortho	..	..	+	Brother and uncle amblyopia
...th eyes, without ...ariotte blindspot	1: both eyes, normal	1: both eyes, normal	Ortho	Ortho	..	..	+	Sister, squint
...both eyes, without ...ariotte blindspot	..	1: both eyes, normal	Ortho	15	..	..	+	Brother, squint; patient's eyes always straight
...both eyes, normal ...th eyes, without ...ariotte blindspot	..	..	10	20	..	+	..	Convergent squint of 12 degrees; father and brother, squint; original vision 6/12 and 6/60; orthoptic training 1½ yr.; vision always regresses after vacation
...oth eyes, without ...ariotte blindspot	..	..	Ortho	Ortho	..	..	+	No vergence; mother, high myopic astigmatism

plot a suppression scotoma in the field of vision. He expressed the opinion that the size of the scotoma is not materially affected by an alteration in the intensity of illumination of between 4 and 10 foot candles or a variation in the size of the stimulus of ¼ to 2 degrees at 1 meter. Travers, however, was unfortunately not able to carry out the test on more than 1 child among all his patients studied.

12. Travers, T.àB.: Brit. J. Ophth. **25**:577, 1938.

Since data on the field of vision to be of any important prognostic use should be obtained when the patient is young, their value is of questionable clinical importance. The finding of a scotoma, if it is more or less constant in its location and if it is easily determined by perimetric study, has more significance than ordinary academic interest. It aids in the diagnosis of amblyopia and in the detection of malingering. In a comprehensive study of the malingerer, Cozzoli [13] did not mention the results of perimetric study as even corroborative evidence of amblyopia ex anopsia. If the scotoma were a factor in amblyopia, its study would greatly aid in the prognosis. Amblyopia, like all the other obstacles (vertical imbalance, abnormal correspondence, etc.) which accompany the psychologic condition associated with squint, even when considered cured, may return. Amblyopia due to a scotoma could be considered cured when the latter was not observed by perimeter. One can easily realize the importance of the finding of a scotoma in view of Evans' [10] explanation that improvement in vision in an amblyopic eye from 3/60 to 6/12 is not a real improvement but on the basis of the scotoma means poorer fixation.

We therefore attempted to find out the relative ease in obtaining and evaluating the consistency of visual field studies in our unselected group. A Bjerrum screen was used at 1 meter, our reason for this long range being that with it we could make certain by watching the patient that he was fixing correctly. The illumination was 7 foot candles. A ¼ degree stimulus was used. When there was good fusion and the patient was intelligent, the study was augmented by a stereoattachment to the Bjerrum screen obtained with two fixed mirrors, one on each side of the face, on a table to which was attached a movable chin rest and a movable central double-faced mirror.

The patient fixed the central electric light on the Bjerrum screen attached to the wall. The movable central mirror was so rotated that the central light of the tangent screen was reflected on the center of the fixed mirror. A red lens held before the fixing eye assured the observer that binocular fixation was obtained when the red and the white (fixation light) met.

The examiner took the field of each eye without knowing which eye was the amblyopic one. In a few cases the fields were also taken on an American Optical Company perimeter with a 1 degree stimulus, a 260 mm. radius and a 15 foot candle illumination. About one hundred and thirty-one pairs of fields were taken on the tangent screen. In some cases two or more fields were taken for the same patient either at the same or at different times.

Results of Examination.—In a few isolated cases the fields taken for the patient at different times contradicted one another, but for the

13. Cozzoli, G.: Gior. di med. mil. **85**:588, 1937.

most part the results were consistent and the children seemed to be anxious to cooperate fully. The fields obtained were of several types, varying from the normal to the field with slight peripheral contraction and the field appearing dumbbell-shaped to the extent that the entire Mariotte blindspot was eliminated in the perimetric plotting. The last-named type of field, however, while commonly seen in cases of amblyopia, was not significant, since the two eyes acquired the same type of field. In a few cases in which this type of field was encountered the patient seemed so hesitant about whether or not he saw the stimulus from the 15 degree area and outward (temporally) that we questioned the veracity of the answers we got regardless of how anxious the patient was to assist us. It may be said that with few exceptions (shown in the accompanying tables) the perimetric fields of amblyopic and of normal eyes were alike.

In tables 1 to 4 we have given the data obtained on the visual fields. These were assembled in the tables without knowledge of which eye was the amblyopic one. However, in reviewing the data in an absolutely biased manner and with the knowledge of which was the amblyopic eye, we found that the highest incidence of field changes obtainable was 20 per cent, an incidence hardly high enough to establish a perimetric anomaly as pathognomonic of amblyopia.

It was not possible by the pathologic changes in the field to determine whether the amblyopia was congenital. Furthermore, one half of the 6 patients with subjective symptoms of suppression or scotoma (see "Suppression") showed no change in the perimetric reading. Our review of their cases, even though they form only a small group, makes it appear that determination of the field in the diagnosis and the prognosis of amblyopia is at present of questionable value.

SUPPRESSION

As pointed out by Cantonnet,[14] the use of a blinder, atropine, etc., in cases of squint has shown how often suppression is followed by amblyopia in the covered, good eye.

In some of our cases of amblyopia we were easily able to plot the suppression area by means of the Haitz chart on a stereoscope. With the synoptophore, of course, the suppression area is easily determined. In a few cases the suppression was so marked as to preclude the possibility of obtaining fusion. Disregarding the miscellaneous group, many of whom were normal when examined, we found that 33 per cent of our patients with amblyopia showed suppression in various stages of intensity.

14. Cantonnet, A.; Filliozat, J., and Fombeure, G.: Strabismus, translated by M. Coque, London, M. Wiseman & Co., 1934.

The question has often been raised whether the scotoma in amblyopia ex anopsia is a real scotoma or a "suppression scotoma." It would seem that either the term suggested by Abraham,[15] "pseudoscotoma," since this scotoma is similar to that of hysteria, or "general retinal depression" [10] would be better, for by using such a term one could appropriately separate in one's mind the scotoma due to retinal disease, such as that in toxic amblyopia, from the scotoma in amblyopia ex anopsia with or without squint and with a normal fundus. The subject is involved, particularly in view of the fact that both squint and its complications (amblyopia, suppression, etc.) are psychologic problems. Thus, for example, hysterical amblyopia is occasionally seen, but the condition may go to extremes. Lillie [16] reported a case of hysterical amblyopia, with spastic convergent squint, superimposed on ciliary spasm in a girl of 18.

One wonders whether the contracted field in many cases of amblyopia has not for its basis the contracted field of hysterical amblyopia as described by Cordes and Horner.[17] Hurst and Symns [18] stated the belief that the taking of the perimetric field of a hysterical patient suggests the narrow field to him. Contracted fields were noted among the fields taken for our patients. Some of our patients had in addition subjective symptoms of suppression, and, indeed, 1 had definite subjective symptoms of scotoma.

The following cases are interesting and worthy of mention:

CASE 31.—Patient D. G. complained of "graying and loss of the picture looked at." Three tangent screen fields were obtained, in only one of which the blindspot of Mariotte appeared larger in the amblyopic eye.

CASE 38.—Patient N. L. said, "While I am reading or looking at distance, the letters disappear completely, to return in a few seconds." Two tangent screen fields were obtained; these were normal except for slight cutting superiorly. Two perimetric fields, one with a white and one with a colored object, were normal. Two fields on Haitz cards showed central suppression of 5 degrees and a few scattered areas of suppression.

CASE 40.—Patient M. T. said vision appeared peppery at about the 6/15 line. He persistently missed the center numbers. Use of the tangent screen showed a dumbbell type of field.

CASE 43.—Patient J. B. complained of "spotty vision with sudden blindness," which was relieved by wearing glasses. One tangent screen field was perfectly normal.

CASE 49.—Patient H. N. could not see the middle letters in each row. One tangent screen field showed slight cutting above, as in case 38; also the Mariotte blindspot was possibly slightly larger in the amblyopic than in the normal eye.

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15. Abraham, S. V.: Amblyopia: Classification with Report of Cases, Arch. Ophth. **12**:391 (Sept.) 1934.

16. Lillie, H. I.: Clin. Bull., Mayo Clin. **3**:170, 1922.

17. Cordes, F. C., and Horner, W. D.: Am. J. Ophth. **16**:592, 1933.

18. Hurst, A. F., and Symns, J. L. M.: Brit. J. Ophth. **3**:17, 1919.

CASE 52.—Patient R. P. said that when he read the test charts with the Wollensak-Allscope magnification the letters appeared "spotty." One tangent screen field was taken and found normal.

It is interesting to note that among these 6 patients with subjective symptoms there was 1 as young as 9 years of age. All but 1 obtained fusion, with 2 of the 6 even obtaining stereopsis.

The stages in the development of amblyopia in squint have been mentioned as, successively, single binocular vision, diplopia, suppression of vision in one eye, squint and, finally, amblyopia. It is thought that in squint suppression is brought on to overcome diplopia, to be succeeded finally by amblyopia. Nevertheless we noted a 25 per cent incidence of suppression in our nonsquinting patients with amblyopia. This experience must also have been that of Derby,[19] who almost a half century ago said that amblyopia is not an effort to avoid diplopia but rather, as he expressed it, a freak of nature.

Duke-Elder [20] ascribed the suppression with the resulting cure in cases of the amblyopia of squint to a difference of the dioptric apparatus. The opinion of other workers in the field appears to be that the problem of amblyopia is a purely psychologic one. Summerskill,[21] for example, has called the condition a symptom or psychologic inhibition and said that the presence of any causative or secondary anatomic lesion is conjectural.

OPHTHALMOLOGIC STUDY

Observers investigating the subject of amblyopia ex anopsia have not found any retinal pathologic change to account for the condition. Barr [22] even stated the belief that in some cases of amblyopia first noted after a severe hemorrhage in the body, ophthalmoscopic examination gave normal results.

In all our cases the fundi were normal. We even augmented our studies by the use of an improvised giant ophthalmoscope. With this, in addition to the usual lenses, a red-free and a monochromatic red filter were utilized. Provision has been made in this ophthalmoscope for use of a monochromatic yellow, green or blue filter if further study is carried out.

ANGLE OF SQUINT

It was interesting to observe how the angle of squint varied when determined at the same sitting on two such reliable instruments as the perimeter and the synoptophore. Considering the amount of prism as

19. Derby, H.: Boston M. & S. J. **116**:186, 1887.

20. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1932, vol. 1, p. 1050.

21. Summerskill, W. H.: Brit. M. J. **1**:1101, 1936.

22. Barr, A. S.: Am. J. Ophth. **17**:396, 1934.

read on the synoptophore as representing in round numbers about 2 degrees and assuming that 5 degrees was too small a difference between the measurements of the two devices to be of importance, we found that 8 patients in group 1 showed a definite variation of 7 to 20 degrees even though the tests were done at the same sitting. The same difference was noted among our adult patients with amblyopia. It may have its explanation in the poor fixation of amblyopia or in the excessive nervous innervation of squint.[23] It seems evident in the face of such discrepancies in figures that it would be best, as shown previously,[1] to make a number of examinations before final judgment is arrived at as to the conditions prevailing in the individual case.

GRADES OF BINOCULAR VISION

Simultaneous Macular Perception.—Even a review of the small series under consideration brings most strikingly to the attention of the ophthalmologist the importance of the early recognition of squint, with its complication amblyopia, and the importance of effecting a cure when possible. In table 1 it may be seen that only 5 of the 26 children who had squint with amblyopia had only simultaneous macular perception. That squint must be a deterrent factor when associated with amblyopia is attested by the fact that none of the patients of group 2 or group 4 had less than fusion. It may be seen in table 3 that among the adults with amblyopia the state of affairs was even worse than that shown in table 1. It is possible that this situation may be accounted for by the fact that the adult patients may have had strabismus in early childhood, untreated, with return of the eyes to parallelism and resultant amblyopia.

Of the 13 patients on whom data are presented in table 3, 3 adults had no simultaneous macular vision whatever. Three patients were not much better, having a low grade. Only 5 patients, less than one half, obtained simultaneous macular vision.

Fusion.—Table 1 reveals that 5 children with squint had no fusion whatever. The fusion of 1 was questionable, of 1 unsteady and of 1 obtained with stimulation. Table 2 reveals that the children in group 2 with the exception of 2 had fusion. These 2 children did get fusion, but it was temporary. Table 3 shows that of our adults with amblyopia only 3 obtained fusion.

Stereopsis.—The highest grade of binocular vision was positively obtained by 6 children of group 1 (table 1). It was questionable whether 3 patients actually had depth perception. Zimmermann,[24] with 27

23. Bielschowsky, A.: Etiology of Strabismus, in Lectures on Motor Anomalies, Hanover, N. H., Dartmouth College Publications, 1940.

24. Zimmermann, H. E.: Klin. Monatsbl. f. Augenh. **100**:600, 1938.

patients, had a slightly better result. He found that 15 had fusion and that 10 had stereopsis as well.

Of the 16 patients in group 2, the children with amblyopia without squint, 8 had stereopsis; 1 is described as having little stereopsis, while the depth perception of 2 was questionable. Five children had no stereopsis.

In group 3, the adults with amblyopia, the situation was most discouraging (table 3). Only 1 patient had stereopsis, and the depth perception of 1 was questioned.

ASSOCIATED OBSTACLES

Amblyopia in itself is in the great majority of cases a difficult condition to treat. When other obstacles are also noted, the prognosis is even less encouraging. Thus we had 1 patient with a "false macula." He had no simultaneous macular perception.

We were more fortunate in our 7 patients with false projection, 6 of whom were improved by treatment. In 1 the false projection was corrected but the permanency of the cure was questioned.

A vertical imbalance ranging from 2 to 6 degrees was noted in 4 of our patients. It was found that 4 had no vergence.

PROGNOSIS

One occasionally hears stories which border on the miraculous regarding patients with amblyopia ex anopsia, wherein loss of sight in the good eye is said to have resulted in the return of normal function to the previously amblyopic eye. Thus, Green [25] reported a case of amblyopia and divergent squint in the right eye in which the vision improved from 6/60 to 6/6 after the destruction of the vision of the good eye by atrophy of the optic nerve. Rosa Ford [26] reported a case of strabismus with amblyopia cured after twenty-nine years by draining of the nasal sinuses. She stated the belief that this amblyopia could not be classed as of the toxic type, since it was caused by pressure on the optic nerve by the edema from the chronic sinusitis. In the majority of cases of amblyopia, however, the cure is far from dramatic.

In a recent review it was found that ordinarily, the maximum time it took to improve our amblyopic patients who did get well was six months.[1] Lyle and Jackson [27] stated correctly that when a patient does not obtain some improvement of vision in six weeks it is best to forego treatment.

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25. Green, A. W.: Brit. M. J. **2**:113, 1935.

26. Ford, R.: Tr. Ophth. Soc. U. Kingdom **53**:507, 1933.

27. Lyle, K., and Jackson, S.: Practical Orthoptics in the Treatment of Squint, London, H. K. Lewis & Co., Ltd., 1937.

Amblyopic patients discharged as cured should be made to return every few months for a recheck. This fact was forcibly demonstrated by 2 patients with squint and amblyopia under our care. Their cases are worthy a short account:

CASE 62.—Patient N. O.'s original vision was 6/9 in the right eye and 6/30 in the left. Training to correct the amblyopia and squint was carried out for one year. The vision in the left eye improved to 6/12. It regressed after a three month vacation to 6/21 and later improved to 6/12.

CASE 67.—Patient M. S.'s original vision was 6/12 in the left eye and 6/60 in the right. She had training for the correction of amblyopia and squint for one and one-half years. The vision improved to 6/6 in the right eye and 6/9 in the left, returning to 6/9 in the right and 6/24 in the left after a vacation.

These cases are interesting in that the vision eventually became normal. We treated the amblyopia longer in them than in any others. The angle of squint, though small, was never corrected. Both patients obtained fusion but no stereopsis.

CONCLUSION

The testing of the vision of 1 patient with different visual charts may elicit different values for visual acuity. When the vision shows a slight variation the cause most likely lies in the fact that what appeals to the eye is read more easily. When, however, the variation is marked the cause more plausibly is that different fixation is used in reading the charts. This definite knowledge of vision is useful in the acceptance and the discharge of an amblyopic patient.

The incidence of scotomas among our amblyopic patients was not as high as that often mentioned in the literature. Suppression areas, however, were common. These areas are not always constant and may be found associated with squint without amblyopia. One can therefore not form a definite opinion from them either as to diagnosis or as to prognosis.

Even though we measured the angle of deviation objectively, using both the synoptophore and the perimeter in each case, a difference in the angle of squint was often obtained.

As would be expected, adults with amblyopia presented the least tendency to cultivate even so little as the first grade of binocular vision. Children with amblyopia without squint showed the best effort, achieving as high as the third grade of binocular vision (depth perception). Amblyopia should be recognized early and every effort made to correct the condition.

TREATMENT OF PNEUMOCOCCIC CORNEAL LESIONS

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SPECIFIC TREATMENT

The specific treatment of pneumococcic corneal ulcers has generally been unsuccessful. During the past four decades various forms of therapy have been enthusiastically proposed, only later to be proved of little value.

The specific remedies may be conveniently divided into three groups: (1) biologic preparations, (2) chemicals other than sulfanilamide and its derivatives and (3) sulfanilamide and its derivatives, particularly sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine).

1. *Biologic Remedies.*—This group includes polyvalent and type-specific antipneumococcus horse serums and the more recently developed type-specific antipneumococcus rabbit serums. Also included are the antipneumococcus vaccines and bacteriophage.

Römer [1] in 1902 first advocated the use of antipneumococcus horse serum in the treatment of corneal ulcers. His recommendation was on the basis of experimentation with rabbits. The clinical results, however, have never been impressive, as has been pointed out by numerous authors, including Axenfeld,[2] Lawford,[3] Verhoeff,[4] Lehrfeld,[5] Cheyney,[6] Wright,[7] Clegg [8] and de Bascarán.[9]

Submitted in partial fulfilment of the requirements for the degree of Doctor of Medical Science in the Faculty of Medicine, Columbia University.

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1. Römer, P.: Experimentelle Grundlagen für klinische Versuche einer Serum-Therapie des Ulcus corneae serpens nach Untersuchungen über Pneumokokkenimmunität, Arch. f. Ophth. **54**:99, 1902.

2. Axenfeld, T.: Serum Therapy in Ophthalmology, Ophth. Rev. **28**:1, 1909.

3. Lawford, J. B.: On Inoculation Treatment in Diseases of the Eye, Tr. Ophth. Soc. U. Kingdom **32**:1, 1912.

4. Verhoeff, F. H.: The Treatment of Hypopyon Keratitis, Tr. Sect. Ophth., A. M. A., 1917, p. 78.

5. Lehrfeld, L.: Serum Therapy as Applied to Pneumococcus Infections of the Eye, New York State J. Med. **106**:214, 1917.

6. Cheyney, R. C.: Types of Pneumococcus Found in Corneal Ulcers, Tr. Internat. Cong. Ophth. **1**:378, 1922.

(Footnotes continued on next page)

The failure may have been due to the fact that corneal ulcers are most often caused by pneumococcic strains of the "higher types," as has been indicated in the reports of Cheyney,[6] Wright,[7] Lobeck,[10] Schmelzer and Eckstein,[11] McKee,[12] Newman[13] and Wood.[14] Only recently, with the development of type-specific antipneumococcus rabbit serums, have antiserums become generally available for the strains beyond types I, II and III. Scheie and Collins[15] reported in 1939 the successful treatment of a patient with ulcus serpens with antipneumococcus rabbit serum.

Antipneumococcus vaccines have been found of little value by a number of investigators, including Römer,[1] Axenfeld[2] and Cheyney.[6] More recently, Rodigina[16] has advocated the use of antipneumococcus bacteriophage in the treatment of corneal lesions.

2. *Chemicals Other than Sulfanilamide and Its Derivatives.*—Prior to the development of sulfanilamide, ethylhydrocupreine was the chief chemical used in the eye against Diplococcus pneumoniae. Ethylhydrocupreine was introduced as a specific treatment for pneumococcic infection by Morgenroth and Levy[17] in 1911. Since the demonstration of its toxic features by Moore and Chesney,[18] the systemic use of this drug has largely fallen into discard. A number of authors, including

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7. Wright, R. E., in Etiology and Treatment of Hypopyon Ulcer Symposium, Tr. Ophth. Soc. U. Kingdom **47**:72, 1927.

8. Clegg, J. G., in Etiology and Treatment of Hypopyon Ulcer Symposium, Tr. Ophth. Soc. U. Kingdom **47**:24, 1927.

9. de Bascarán, A.: La úlcera serpiginosa de la córnea y su tratamiento por las sulfamidas, Semana méd. españ. **3**:409, 1940.

10. Lobeck, E.: Zur Frage der Pneumokokken infektionen am Auge, Arch. f. Ophth. **127**:395, 1931.

11. Schmelzer, H., and Eckstein, E.: Die augenpathogene Bedeutung der Streptokokken und Pneumokokken (547 Untersuchungen), Arch. f. Ophth. **132**:24, 1934.

12. McKee, S. H.: A Study of the Pneumococcus Group from the Inflamed Conjunctiva and Lacrimal Sac, Am. J. Ophth. **18**:1021, 1935.

13. Newman, E. W.: Diplococcus Pneumoniae and Streptococcus Viridans in Ocular Disease, Arch. Ophth. **19**:95 (Jan.) 1938.

14. Wood, M.: A Study of the Methemoglobin-Producing Organisms in Ocular Inflammations, Am. J. Ophth. **22**:1111, 1939.

15. Scheie, H. G., and Collins, L. H., Jr.: Use of Rabbit Antipneumococcus Serum in Treatment of Ulcus Serpens, J. A. M. A. **112**:2130 (May 27) 1939.

16. Rodigina, A. M.: Pneumococcic Bacteriophage: Its Application in the Treatment of Ulcus Serpens Corneae, Arch. Ophth. **19**:81 (Jan.) 1938.

17. Morgenroth, J., and Levy, R.: Chemotherapie der Pneumokokkeninfektion, Berl. klin. Wchnschr. **48**:1560, 1911.

18. Moore, H. F., and Chesney, A. M.: A Study of Ethylhydrocupreine (Optochin) in the Treatment of Acute Lobar Pneumonia, Arch. Int. Med. **19**: 611 (April) 1917.

Goldschmidt,[19] Rieger,[20] Arruga,[21] Burch [22] and Gifford,[23] have continued to recommend its local use in the treatment of pneumococcic corneal ulcers. However, McKee,[24] de Bascarán,[9] Hutchinson [25] and others have said that the value of this drug is equivocal.

Sabatzky [26] and McKee [24] have suggested the use of methyl salicylate as a specific cauterizing agent in the treatment of ulcus serpens, but Koldovsky-Kvetoslav [27] found the method without merit.

3. *Sulfanilamide and Its Derivatives.*—With the development of sulfanilamide and more particularly the sulfapyridine derivative, it was hoped that these chemicals might indeed prove to be the real specific for pneumococcic corneal ulcers.

A number of clinical reports have appeared suggesting some benefit from the use of sulfanilamide or sulfapyridine.

Roggenkämper [28] in 1939 reported treating 15 serpent ulcers with azosulfamide with remarkable healing, but no bacteriologic studies were included. Bailey and Saskin [29] recorded the control of hypopyon ulcer with sulfanilamide, but again the cause of the ulcer was not determined.

De Bascarán [9] reported satisfactory healing in 10 cases of hypopyon ulcer treated with azosulfamide locally or with the original prontosil (a hydrochloride of 4′-sulfonamido-2,4-diaminoazobenzene) by mouth. This treatment was in addition to other forms of therapy, including cauterization and instillation of ethylhydrocupreine. However, in no instance were bacteriologic studies made.

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19. Goldschmidt, M.: Experimentelle Studien über Diffusion durch die Hornhaut. Diffusen und Iontophorese des Optochins des Zinksulfats, Arch. f. Ophth. **103**:280, 1920.

20. Rieger, H.: Zur Stargardtschen Prophylaxe des Ulcus serpens mit Optochin, Ztschr. f. Augenh. **67**:215, 1929.

21. Arruga, R.: Sobre el tratamiento de la úlcera serpiginosa de la córnea con la iontoforesis de optoquin, Arch. de oftal. hispano-am. **30**:327, 1930.

22. Burch, F. E.: General and Local Treatment, in Berens, C.: The Eye and Its Diseases, Philadelphia, W. B. Saunders Company, 1936, p. 1001.

23. Gifford, S. R.: A Hand-Book of Ocular Therapeutics, Philadelphia, Lea & Febiger, 1937, p. 51.

24. McKee, S. H.: Treatment of Serpiginous Ulcer of the Cornea with Methyl Salicylate, Arch. Ophth. **21**:121 (Jan.) 1939.

25. Hutchinson, B. B.: Hypopyon Ulcer, Texas State J. Med. **36**:40, 1940.

26. Sabatzky, K.: Eine neue Methode zur raschen Heilung des Ulcus serpens mit Erhaltung der Durchsichtigkeit der Hornhaut, Klin. Monatsbl. f. Augenh. **83**:498, 1929.

27. Koldovsky-Kvetoslav: Wintergreen Oil as a Remedy in Ulcers of the Cornea, Oftal. sborn. **5**:193, 1930; abstracted, Am. J. Ophth. **15**:76, 1932.

28. Roggenkämper, W.: Hornhautulkus und Prontosil, Klin. Monatsbl. f. Augenh. **103**:211, 1939.

29. Bailey, J. H., and Saskin, E.: Treatment of Severe Corneal Ulcer with Sulfanilamide, Arch. Ophth. **22**:89 (July) 1939.

Rosengren [30] described the beneficial results of treating 6 patients with ulcus serpens with sulfapyridine, but in only 2 instances were there smears positive for lancet-shaped diplococci and in none was the microorganism typed. Szinegh [31] treated 10 patients with classic serpiginous ulcer with sulfapyridine for periods of five to seven days. Progression of the lesions was apparently controlled and scarring reduced, but again no proof of a pneumococcic etiologic agent was obtained.

Guyton [32] listed a case of panophthalmitis due to D. pneumoniae type II treated with sulfapyridine but ending with evisceration after three days. He also described a case of pneumococcic corneal ulcer associated with conjunctivitis which was benefited by sulfapyridine treatment by mouth for seven days.

When one considers these reports it is apparent that the tendency for a number of ulcers to heal with nonspecific treatment must not be overlooked.

In a few clinical cases of proved pneumococcic hypopyon keratitis treated with sulfapyridine at the New York Eye and Ear Infirmary and at the Institute of Ophthalmology of the Presbyterian Hospital the results have not been conclusive.

In view of the destructive character of pneumococcic corneal lesions and their frequency, particularly in industrial areas, it was considered worth while to attempt an experimental evaluation of sulfapyridine therapy.

PRELIMINARY INVESTIGATIONS

The major difficulty encountered in setting up the experiment was that of producing a standard corneal lesion. Albino rabbits were selected as the most satisfactory animals in which to establish an experimental pneumococcic ulcer.

It was hoped that a simple means of inoculation could be utilized which would be comparable to the corneal abrasion which often precedes clinical hypopyon keratitis in man. However, it was found that the uniformity of lesions acquired by merely abrading the cornea with an infected instrument was not sufficient to meet the requirements of a standard lesion.

An intracorneal injection method was finally devised whereby a standard wheal dose of the inoculum could be injected into the corneal

30. Rosengren, B.: Treatment of Ulcus Serpens Corneae with M. & B. 693, Acta ophth. **17**:209, 1939.

31. Szinegh, B.: Der Wert der Chemotherapie in der Behandlung des Ulcus serpens corneae, Arch. f. Ophth. **141**:300, 1939.

32. Guyton, J. S.: The Use of Sulfanilamide Compounds in Ophthalmology, Am. J. Ophth. **22**:833, 1939.

stroma, a no. 27 gage hypodermic needle and a tuberculin syringe being used. The material for inoculation consisted of a saline suspension of heart's blood of a mouse dying with pneumococcic septicemia. In this mixture approximately 0.25 cc. of blood was added to 0.50 cc. of saline solution. The strains of D. pneumoniae used were type VI and type XIX, each of which was isolated from a clinical patient with hypopyon keratitis. The virulence of these organisms was maintained by frequent mouse passages in which the blood of one mouse dying with pneumococcic septicemia was injected into the peritoneal cavity of the succeeding mouse.

It was found that an injection into the cornea of a mixture of sterile blood and saline solution produced only a slight reaction, as may be seen in figure 1*A*. This was in contrast to the severe ulceration seen

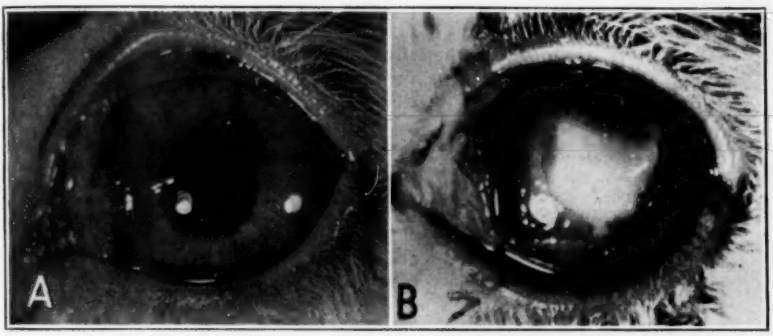

Fig. 1.—*A*, reaction to an injection of a saline suspension of sterile blood. *B*, reaction to an injection of pneumococcus inoculum.

in figure 1*B*, which followed the intracorneal injection of pneumococcus inoculum. The photographs were taken four days after inoculation.

By this method of injection a uniform corneal lesion was obtained, in which the reaction of the eyelids and conjunctiva, the corneal ulceration and infiltration and the presence of hypopyon were comparable in many respects to those of the pneumococcic keratitis seen in the clinic.

ORGANIZATION OF EXPERIMENTS

The rabbit experiments testing the efficiency of the administration of sulfapyridine by mouth in the treatment of pneumococcic corneal lesions were carried out in six series. The animals used were albino rabbits weighing usually between 2,000 and 2,500 Gm. Prior to inoculation topical anesthesia was obtained with 1 per cent pontocaine, and the intracorneal injection was made obliquely into the stroma in the manner

which has been described. The approximate number of micro-organisms injected was determined by making pour plate blood agar cultures of significant dilutions of the inoculum.

The sulfapyridine powder [33] was administered by stomach tube in series 1, while in the succeeding experiments the powdered drug was mixed with water in such proportions that each dose was contained in 5 cc. of the suspension. The mixture was given through a graduated 10 cc. pipet with a protective rubber tip which could be inserted well back into the animal's pharynx. This method of administration was found to be satisfactory and much less arduous for the animals than other methods.

In the first experimental series a dose of 0.3 Gm. twice daily was selected because previous experience had seemed to indicate a toxicity of sulfapyridine repeatedly administered in larger quantities. In view of the relatively low levels of sulfapyridine in the blood attained, the dose was increased successively in the subsequent experiments to a maximum dose of 1.2 Gm. repeated twice daily in series 4. As it was considered important to insure a constant therapeutic level of sulfapyridine throughout the day and night, the routine was changed in series 5 and 6 to 1.2 or 1 Gm. given every eight hours, or three times daily. The marked irregularity in the absorption of sulfapyridine by rabbits has been pointed out by Long and Bliss,[34] and many instances of this erratic behavior were encountered in these experiments. For this reason no attempt was made to calculate for each animal an individual dose on the basis of body weight.

In series 1 the treatment was not started until eighteen hours after inoculation, an interval being allowed to permit the corneal lesions to become well established before the beginning of therapy. However, in view of the severe lesions obtained and the absence of an appreciable difference between the treated and the untreated animals, the therapy in series 2 was begun only thirty minutes after inoculation. In the remaining four series of experiments the initial dose was given at least five hours before corneal inoculation. This was done to bring out the maximum effect of the drug. Treatment was continued in each instance throughout the acute phase of the lesion or for at least eight days.

Material for culture was taken from the corneal lesions daily, usually on rabbit's blood agar plates with dry swabs. The cultures were repeated until two negative ones had been obtained.

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33. The sulfapyridine used was supplied by Merck & Co., Rahway, N. J.

34. Long, P. H., and Bliss, E. A.: The Clinical and Experimental Use of Sulfanilamide, Sulfapyridine and Allied Compounds, New York, The Macmillan Company, 1939, p. 79.

In the later experiments at least two determinations of the sulfapyridine in the blood were made for each animal. Between four and five hours after feeding of the drug, blood samples were withdrawn from an ear vein and transferred to oxalate tubes. The estimations were made by Dr. Karl Meyer [35] and associates at the Institute of Ophthalmology of the Presbyterian Hospital, the colorimetric method of Marshall [35a] being used.

Daily observations of the corneal lesions were recorded during the acute phase, followed by readings at longer intervals as the lesions became quiescent. Measurements were made in millimeters when feasible and were supplemented by a + to + + + + system of estimation. Features noted in the examination included the general condition of the animal, the extent of the swelling of the lid and the conjunctivitis and the amount and character of the discharge. In the cornea proper the millimeters of ulceration and the extensiveness of the surrounding infiltration were observed. The presence of hypopyon and the amount of circumcorneal reaction were likewise recorded. For purposes of comparison tables were prepared which presented the observations made on each animal (1) at the peak of the acute phase on the third day after inoculation, (2) on the ninth day, when the reaction was beginning to subside, and (3) at the end of three weeks, as the lesions became quiescent.

A total of 49 animals were successfuly inoculated and observed at least through the acute phase of ulceration. This total does not include a number of animals lost apparently through the toxicity of the drug, particularly in series 5 and 6.

The final series is here presented in detail to indicate the procedures followed and to illustrate the significant findings. The results of the other experiments are considered in the comment and the summary.

SERIES VI: TREATMENT OF EXPERIMENTAL PNEUMOCOCCIC CORNEAL LESIONS WITH SULFAPYRIDINE

Animals.—Albino rabbits of 2,450 to 3,200 Gm. were selected.

Inoculum.—A heavy saline suspension was made of heart's blood of a mouse dying with type XIX pneumococcus septicemia. This mixture consisted of approximately 0.25 cc. of heart's blood and 0.5 of saline solution. By making blood agar pour plate cultures of significant dilutions of this inoculum and counting the colonies grown, it was estimated that each injection of 0.03 cc. contained

35. Meyer, K.; Bloch, H. S., and Chamberlain, W. P., Jr.: The Distribution of Sulfapyridine Between Blood, Aqueous Humor and Cornea, Am. J. Ophth. **24**:60, 1941.

35a. Marshall, E. K., Jr., and Litchfield, J. T.: The Determination of Sulfanilamide, Science **88**:85, 1938.

approximately 200,000,000 organisms (D. pneumoniae). This type XIX strain was originally isolated from a clinical patient with hypopyon keratitis.

Procedure.—Rabbits 503, 504, 505, 510, 511, 512, 501, 502, 507 and 508 were given intracorneal injections in the left eye of approximately 0.03 cc. of pneumococcus inoculum.

Treatment.—The powdered sulfapyridine was administered by pipet in the manner described. The administration beginning five hours before inoculation, rabbits 503, 504, 505, 510, 511 and 512 received 1.2 Gm. of sulfapyridine for a total of three doses. The dose was then decreased to 1 Gm. three times daily at

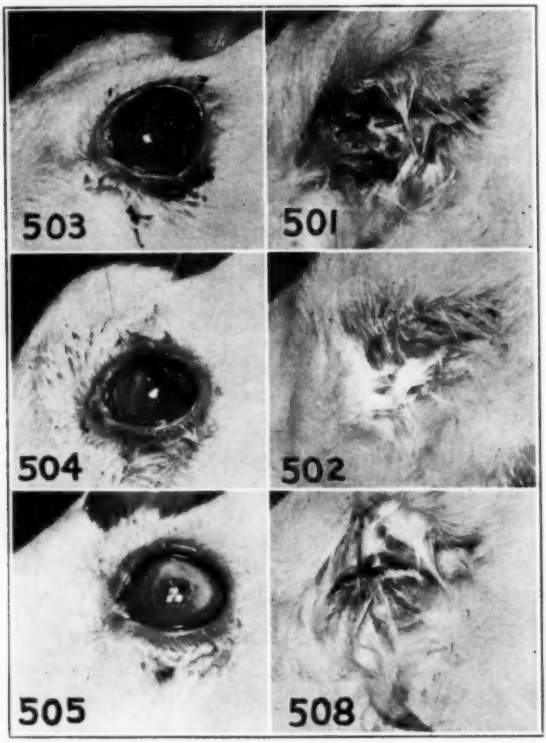

Fig. 2 (series 6).—Appearance the third day after inoculation.

intervals of eight hours. Therapy was continued through the eighth day. Rabbits 501, 502, 507 and 508 were reserved as controls.

Results.—On the third day after inoculation, at the peak of the acute phase of corneal ulceration, there was a striking difference between the control animals and those which had received the drug. The lids were completely closed with swelling and the lashes were matted together with exudate in each of the untreated animals (fig. 2). The corneal infiltration and circumcorneal injection were likewise much more marked than in the treated animals (table 1).

By the ninth day, however, the extensive reaction of the adnexa which had been observed in the control animals had largely subsided (table 2). While the corneal lesions were still somewhat more severe

TABLE 1.—*Status of the Lesions on the Third Day in Series 6*

	Sulfapyridine-Treated Rabbits						Untreated Rabbits			
Rabbit number	503	504	505	510	511	512	501	502	507	508
Adnexa										
Lids	+	++	+	+	+	++	++++	++++	++++	+++
		—				—	—	—	—	
Conjunctiva	+	++	+	++	+	++	++++	+++	++++	+++
		—					—		—	
Discharge	+	++	+	+	+	+	++++	+++	++++	++++
		—								
Cornea										
Extent of abscess, mm.	6.5	8	9	9	7	7		Not measurable		
	6	7	7	7	6	6				
Extent of infiltrate	++	++	++	++	++	++	+++	+++	+++	+++
					—	—				
Pannus, mm	0	0	0.25	0	0	0	0	0	0	0
Perforation	0	0	0	0	0	0	0	0	0	0
Iris										
Ciliary injection	++	+++	++	++	++	++	+++	+++	+++	++++
	—									—
Hypopyon, mm	2	3	2	1	2	3		Not visible		

TABLE 2.—*Status of the Lesions on the Ninth Day in Series 6*

	Sulfapyridine-Treated Rabbits						Untreated Rabbits			
Rabbit number	503	504	505*	510*	511	512*	501	502	507	508
Adnexa										
Lids	+	+	..	..	++	..	++	+	++	++
	—				—					—
Conjunctiva	+	++			++		++	++	++	++
		—						—		
Discharge	+	+			++		++	+	++	++
							—	—		—
Cornea										
Extent of abscess, mm.	5.5	8			12		9	7	Not mea-	8
	3.5	6			10		7	6	surable	6
Extent of infiltrate	++	+++			++		++	++	++	++
	—	—								
Pannus, mm	3	2.5			1.5		3	3	2.5	3
Perforation	0	0			0		0	0	0	0
Iris										
Ciliary injection	++	++			++		++	++	++	++
Hypopyon, mm	0	0			3		Not visible	3.5	0	3

* Died.

in the control group than in the treated animals, the differences had become less pronounced (fig. 3). The same general similarity of lesions in the treated and the untreated group persisted on the nineteenth day (table 3).

Table 4 presents the results of cultures of material taken from the corneal lesions with sterile dry swabs and streaked on rabbit's blood agar plates. All cultures were negative after the third day in this series, and there was no appreciable difference between treated and untreated animals as to persistence of positive cultures.

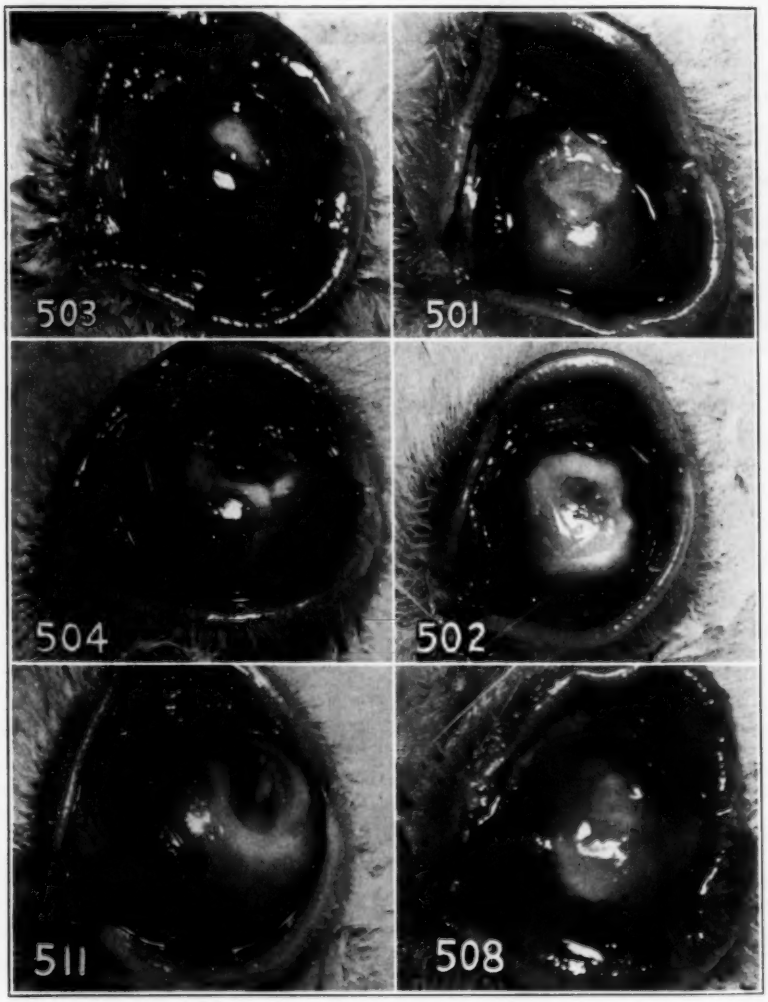

Fig. 3 (series 6).—Appearance the tenth day after inoculation.

Two determinations of the level of sulfapyridine in the blood were obtained for each animal (table 5). Sample 1 was taken on the first day after inoculation, when the rabbits were receiving 1.2 Gm. of sulfa-

pyridine at eight hour intervals. From sample 2 more reasonable concentrations in the blood were reported, with the individual dose reduced to 1 Gm.

TABLE 3.—*Status of the Lesions on the Nineteenth Day in Series 6*

	Sulfapyridine-Treated Rabbits						Untreated Rabbits			
Rabbit number	503	504	505*	510*	511	512*	501	502	507*	508
Adnexa										
Lids	+	++			++		+	+		++
Conjunctiva	++	++			++		+	+		++
	—	—			—			—		—
Discharge	+	++			++		+	++		++
		—			—			—		
Cornea										
Extent of scar, mm	4	6			7		3	5.5		3.5
Extent of infiltrate	2	5.5			6		2.5	2.5		2.5
Pannus, mm	4.5	5.5			5.5		5.5	5.5		5.5
Perforation	0	+			0		+	0		+
Iris										
Ciliary injection	+	+			++		+	+		0.25
Hypopyon	0	0			0		0	0		0

* Died.

TABLE 4.—*Cultures from Corneal Lesions, Series 6*

		Number of Days				
	Rabbit	1	2	3	4	5
Treated	503	+	+	—	—	
	504	+	—	+	—	—
	505	+	—	—	—	
	510	+	—	—	—	
	511	—	—	—		
	512	+	—	+	—	—
Untreated	501	+	—	—		
	502	+	+	+	—	—
	507	+	—	—		
	508	+	+	—	—	

TABLE 5.—*Levels of Sulfapyridine in the Blood,* Series 6*

	Sample No.	Dose of Drug	Rabbit					
			503	504	505	510	511	512
First day	1	1.2 Gm. t.i.d.	20	28.6	20.0	16.7	18.2	3.3
Fourth day	2	1.0 Gm. t.i.d.	10	11.1	14.3	6.3	5.0	4.0

* Milligrams per hundred cubic centimeters of blood.

SUMMARY OF OBSERVATIONS

The results obtained in each of the six experimental series have been summarized for the three stages selected for comparison.

At the peak of the acute phase, on the third or fourth day, there was no appreciable difference between the treated and the control animals in series 1, 2 and 3. Three of 5 treated rabbits in series 4 showed less

severe corneal lesions than were found in either control. At this stage in series 5 and 6 the untreated animals exhibited marked swelling of the lids and a profuse purulent discharge, which were in sharp contrast to the moderate reaction of the adnexa in animals receiving the drug. Also, there were a less severe corneal lesion and a smaller amount of circumcorneal reaction in the treated animals than in the controls.

The second comparison was made after eight days of oral treatment with sulfapyridine. At this time the animals in series 1 and 3 again displayed no appreciable difference whether treated or untreated. In series 2, 4, 5 and 6 there seemed to be somewhat less severe corneal lesions in the animals that received sulfapyridine. At this time the extensive reaction of the adnexa previously seen in control rabbits in series 5 and 6 had largely subsided, so that it was no longer a distinguishing feature.

The relative healing was again checked approximately three weeks after inoculation. In series 2 the residual corneal lesions of 2 of the 4 surviving treated animals were less marked than those of the controls. Similarly, in series 3 and 4, 2 of the 5 treated rabbits exhibited less extensive lesions than those present in the corresponding controls. In series 5 and 6 there were slightly less severe residual corneal lesions in the animals that received the drug. Observations made again at the end of two and of three months showed the same general relation between treated and untreated groups.

Determinations of Sulfapyridine in the Blood.—In series 2 the levels of sulfapyridine varied between 2 and 14 mg. per hundred cubic centimeters. Although the dose administered was slightly higher in series 3, the figures were between 0.57 and 5.9 mg. per hundred cubic centimeters. Levels of sulfapyridine in the blood of 2.5 to 20 mg. were encountered in series 4, with only two values for a total of fifteen samples falling below 4 mg. per hundred cubic centimeters. With the same large doses of the drug administered at eight hour intervals, the levels in series 5 fell between 5 and 33.3 mg. and in series 6 between 3.3 and 28.6 mg. per hundred cubic centimeters. From these values it may be seen that, particularly in series 4, 5 and 6, an adequate content of free sulfapyridine was apparently present in the blood stream.

Cultures of Material from Corneal Lesions.—Systematic daily cultures were made of material from the corneal lesions in all experiments except those in series 1. In series 2 the cultures for the treated animals were negative after the second day, whereas the cultures of the 2 control animals were positive for three and four days, respectively. Contrasted with this are the findings in series 4, in which all the controls had negative cultures after two days, while 1 of the treated animals had positive cultures for four days after inoculation. In series 3, 5 and 6 there was no significant difference between treated and untreated animals as to length of time cultures were positive.

COMMENT

The most striking result of the treatment with sulfapyridine was the marked reduction in the reaction of the adnexa during the acute phase in series 5 and 6. In the animals in these experiments, receiving large doses of the drug at eight hour intervals, the corneal lesions were, however, only moderately less severe than those present in the corresponding controls. Even with treatment instituted prior to inoculation, the beneficial effects with regard to the corneal infection proper were somewhat disappointing.

In an attempt to explain the reduced efficiency of sulfapyridine in dealing with pneumococcic lesions of the cornea, a number of factors were considered. Repeated determinations showed that in most instances the blood concentration of free sulfapyridine was well within the recommended therapeutic range. Although the animals in series 4 had well tolerated doses of 1.2 Gm. twice daily, this amount repeated at eight hour intervals in series 5 and 6 produced excessive levels up to 33 mg. of sulfapyridine per hundred cubic centimeters. These high concentrations of the drug probably contributed largely to the mortality encountered in the latter two series. It was believed important, however, to obtain the highest possible concentration of the drug because of the failure of smaller doses to be effective.

In view of the fact that certain strains of D. pneumoniae may be relatively resistant to sulfapyridine therapy, it was considered worth while to check with mice the protective power of sulfapyridine against the organisms employed (D. pneumoniae type VI). Standard white mice were given intraperitoneally injections of dilutions of pneumococcus broth culture, essentially the routine reported by Whitby [36] in his initial experiments being used. The high virulence of this pneumococcic strain was evidenced by the fact that approximately one organism was sufficient to kill an untreated animal in about two and one-half days. On the other hand, sulfapyridine was able to protect against 31,500 times this minimal lethal dose for at least three days beyond the four day treatment period. This would seem to indicate that this strain of D. pneumoniae was readily susceptible to the inhibiting action of sulfapyridine.

Finally, the mode of action of sulfapyridine was considered in the attempt to explain why the drug was not more efficient in the treatment of pneumococcic corneal ulcers. A consensus seems to favor the conception that sulfanilamide derivatives are primarily bacteriostatic rather than bactericidal in their action. Through the reaction of the drug, or one of its components, with some essential substance of the bacterium, the micro-organism loses its power to reproduce rapidly and invade the

36. Whitby, L. E. H.: Chemotherapy of Pneumococcal and Other Infections with 2-(*p*-Aminobenzenesulfonamido) Pyridine, Lancet **1**:1210, 1938.

host. This bacteriostasis permits the normal defenses of the body, particularly phagocytosis, to become effective in actually destroying the remaining pathogenic organisms.

As Duke-Elder [37] has emphasized, the cornea is a compact and avascular tissue in which these defense mechanisms are not readily mobilized. Hence, it might be expected that an agent which is primarily bacteriostatic would produce less dramatic effects in the cornea than in a highly vascular structure such as the lung.

In conclusion, an analogy may be drawn between the ulcer or abscess of a pneumococcic corneal lesion and the empyema abscess following pneumococcic pneumonia. Long and Bliss [38] early noted that sulfapyridine therapy was not successful in sterilizing empyema cavities. Lockwood, Coburn and Stokinger [39] also observed that the presence of quantities of cellular debris in any lesion rendered the drug less effective. Fox [40] demonstrated that the addition of sulfapyridine to empyema fluid in vitro did not inhibit the growth of D. pneumoniae in this medium. These findings indicate the presence of some substance in necrotic debris which counteracts the action of the drug. It is interesting to note that in a deeply invasive purulent pneumococcic corneal ulcer many of the same conditions prevail. This may explain in part the failure of certain pneumococcic corneal lesions to be controlled by sulfapyridine even in the presence of an adequate concentration of the drug in the tissue of the cornea.

CLINICAL TREATMENT OF PNEUMOCOCCIC CORNEAL ULCERS WITH SULFAPYRIDINE

A number of clinical reports dealing with the treatment of pneumococcic corneal ulcers with sulfapyridine have already been mentioned. In almost none of the cases reported was there a proved pneumococcic etiologic agent, and rarely was the concentration of the drug in the blood studied.

The following cases of corneal ulcer treated with sulfapyridine were observed at the New York Eye and Ear Infirmary or at the Institute of Ophthalmology of the Presbyterian Hospital during the years 1939 and 1940. In each instance the diagnosis of corneal ulcer due to D. pneumoniae was established by the typing of the organism cultured from the lesion. The typing procedure was carried out according to the

37. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1938, vol. 2, p. 1809.

38. Long and Bliss,[34] p. 233.

39. Lockwood, J. S.; Coburn, A. F., and Stokinger, H. E.: Studies on Mechanism of Action of Sulfanilamide: Bearing of Character of Lesion on Effectiveness of Drug, J. A. M. A. **111**:2259 (Dec. 17) 1938.

40. Fox, C.: Personal communication to the author, 1941.

Neufeld technic as described by Cooper and Walter.[41] In most of the cases determinations of the sulfapyridine in the blood were made.

Although the number of these clinical cases is not large, they are of interest in view of the comparable results obtained in the treatment of the experimental lesions in rabbits.

Case 1.—P. S., a 48 year old Italian man, was admitted to the New York Eye and Ear Infirmary on Nov. 13, 1939. A history was obtained of his having been struck in the left eye with a twig nine days previously. He had noted redness, pain and tearing of increasing intensity. Examination of the left eye showed swelling of the lids, chemosis of the conjunctiva and a purulent discharge. An extensive ulcer with a necrotic base and undermined edges occupied the central one third of the cornea. The lacrimal passages were free of obstruction. Smears taken from the ulcer showed gram-positive lancet-shaped diplococci. On culture D. pneumoniae type XXXI was isolated. Sulfapyridine treatment by mouth was begun on the first day after admission to the hospital, a dose of 1 Gm. being given every six hours. This routine was continued for seven days.

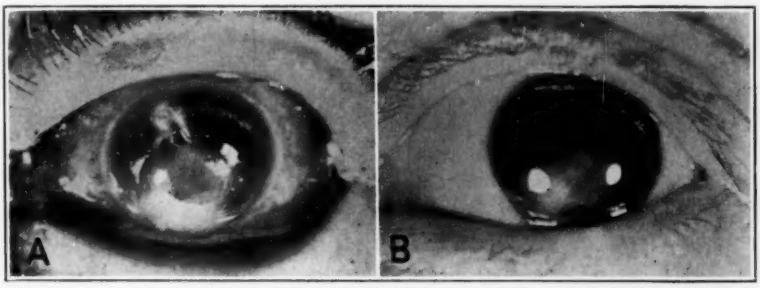

Fig. 4 (case 1).—*A*, hypopyon keratitis (D. pneumoniae type XXXI). *B*, healed ulcer.

Local treatment included the use of atropine and hot baths and the instillation of 2 per cent ethylhydrocupreine hydrochloride solution four times a day. The patient also received 5,000,000 killed bacilli (Bacillus typhosus) intravenously. Despite energetic treatment, the area of ulceration increased rapidly, particularly at its upper border (fig. 4 *A*). On the fifth day the advancing margin was treated with the actual cautery. On the sixth day a slow process of healing began which resulted in central macular corneal opacities of moderate density (fig. 4 *B*). The vision was reduced to 4/200 in the left eye and was not improved with lenses.

Case 2.—G. C., a 63 year old Italian man, was admitted to the Institute of Ophthalmology of the Presbyterian Hospital on June 3, 1940. A history was obtained of redness, swelling and pain in the left eye of ten days' duration. Examination revealed a central corneal ulcer with a hypopyon of 4 mm. The lacrimal sac was obstructed, and purulent material could be expressed. Smears taken from the ulcer revealed gram-positive lancet-shaped diplococci. On culture D. pneumoniae type XIII was isolated. Sulfapyridine therapy by mouth was begun on the day of entry, with doses of 0.6 Gm. every four hours; this amount

41. Cooper, G. M., and Walter, A. W.: Application of the Neufeld Reaction to the Identification of Types of Pneumococci, Am. J. Pub. Health **23**:469, 1935.

was later altered according to the blood content of sulfapyridine, which averaged 7.7 mg. per hundred cubic centimeters. Chemotherapy was continued for eleven days. Local treatment included the use of atropine 1 per cent and frequent hot applications. The lacrimal sac was removed. The hypopyon disappeared on the first day after admission, but the epithelization progressed slowly and irregularly. The eye was red, and there was still intermittent staining of the cornea two months after admission. A dense central leukoma gradually developed, with posterior corneal deposits and iridic adhesions. No useful vision remained.

Case 3.—M. C., a 64 year old Italian man, was admitted to the New York Eye and Ear Infirmary on May 14, 1940. A history was obtained of the left eye's being struck with a twig seven days previously. The blow was followed by increasing irritation, redness and photophobia. Examination showed a central corneal ulcer 5 mm. in diameter, with infiltrated borders. A hypopyon of several millimeters was present (fig. 5 *A*). The lacrimal passages were free of obstruction. Smears taken from the ulcer showed gram-positive lancet-shaped diplococci; D. pneumoniae type XXVIII was isolated on culture. Sulfapyridine therapy by mouth was instituted on the third day, with two initial doses of 1.5 Gm. at four

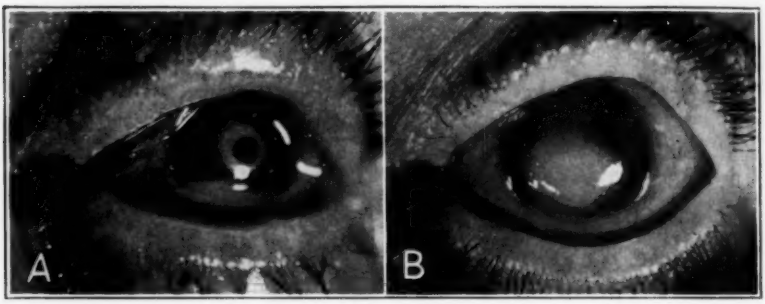

Fig. 5 (case 3).—*A*, hypopyon keratitis (D. pneumoniae type XXVIII). *B*, healed ulcer.

hour intervals followed by a routine of 1 Gm. every six hours for nine days. A level of sulfapyridine in the blood of 6.3 mg. per hundred cubic centimeters was recorded. Local treatment included the use of atropine and hot baths. A paracentesis was performed on the sixth day, and the anterior chamber was irrigated. Despite energetic treatment, the ulcer increased to 5.5 by 6.5 mm. in size and cultures remained positive for D. pneumoniae type XXVIII through the sixth hospital day. Finally, after a protracted period of healing, a dense central leukoma was formed with a posterior iris synechia and complicated cataract. The vision was reduced to perception of hand movements in this eye (fig. 5 *B*).

Case 4.—A. E., a 62 year old Lithuanian-Jewish man, was admitted to the New York Eye and Ear Infirmary on Aug. 25, 1940. He gave a history of pain, redness and irritation in the right eye of four days' duration. Examination disclosed a central corneal ulcer 5 by 4 mm. in diameter. A hypopyon of 1.5 mm. was present. The lacrimal sac was free of obstruction. Smears obtained from the ulcer showed gram-positive diplococci which were not lancet shaped. In the culture was isolated D. pneumoniae type III. The patient received local treatment including the use of atropine and hot applications and the injection of 5,000,000 killed bacilli (B. typhosus) intravenously. Sulfapyridine treatment was not begun

until the third hospital day, when an initial dose of 2 Gm. was administered; this was followed by 1 Gm. every six hours for five days. A determination of the sulfapyridine in the blood showed 6.5 mg. per hundred cubic centimeters. From the first day after admission there was steady progression of healing. At the time the use of sulfapyridine was started, the staining area had already been reduced by one half. The hypopyon disappeared in five days, and epithelization was complete in nine days, with only moderate corneal scarring.

Case 5.—J. S., a 73 year old Irishman, was admitted to the New York Eye and Ear Infirmary on Aug. 28, 1940. He gave a history of redness and pain in the left eye of three weeks' duration. Examination disclosed a central corneal ulcer with an advancing nasal border (fig. 6). A 2 mm. hypopyon was present. The lacrimal passages were free from obstruction. Smears taken from the ulcer revealed gram-positive lancet-shaped diplococci. D. pneumoniae type XXIII was isolated on culture. On the day of admission the actual cautery was applied to the ulcer and paracentesis performed to remove the hypopyon. Sulfapyridine therapy was started immediately, a dose of 1 Gm. being given every six hours. This amount was reduced to 0.6 Gm. on the second day, and the administration

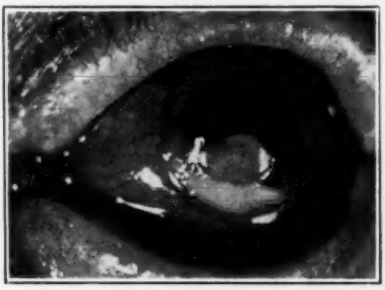

Fig. 6 (case 5).—Hypopyon keratitis (D. pneumoniae type XXIII).

was continued for a total of six days of treatment. A determination of the sulfapyridine in the blood showed 5.4 mg. per hundred cubic centimeters. A small central descemetocele developed, but there was no perforation. The cornea gradually healed, a fairly dense vascularized scar forming over the central and lower portions.

Case 6.—J. M., a 69 year old Italian man, was admitted to the Institute of Ophthalmology of the Presbyterian Hospital on May 31, 1939. He gave a history of pain, redness and tearing of the right eye of three weeks' duration. Examination showed a peripheral corneal ulceration extending nearly half way around the cornea on the nasal side. Smears revealed a few gram-positive cocci in pairs. On culture D. pneumoniae type XVI was isolated. Sulfapyridine treatment was instituted by mouth at the time of admission, a dose of 0.6 to 1.0 Gm. being given every six hours. The dose was later altered according to the sulfapyridine concentration in the blood, which varied from 2.7 to 11 mg. per hundred cubic centimeters. There was progressive healing of the ulcer, terminating in a vascularized leukoma of moderate density.

Analysis of Cases.—Six cases of pneumococcic corneal ulcer have been presented, in each of which the etiologic agent was confirmed by

the typing of D. pneumoniae. In 5 of these cases there was an extensive central ulcer with associated hypopyon. The sixth case was of a marginal corneal ulcer with no exudate in the anterior chamber. Each patient received sulfapyridine by mouth in doses of 0.6 to 1 Gm. at six hour intervals. In all except the first case determinations were made of the level of sulfapyridine in the blood.

In cases 1 and 3 there was definite progression of the ulcer for approximately four days after sulfapyridine treatment had been instituted. In case 4 the ulcer had already begun to heal when treatment with the drug was started. In cases 1, 2, 3 and 5 the resultant corneal scarring was sufficient to destroy useful vision.

To summarize, the sulfapyridine may have been beneficial in case 1 in reducing the density of the scar, although it failed for four days to halt the progression of the lesions. In cases 4 and 6 there may have been some effect in speeding the recovery, though there is an impression that the ulcers might have healed as well with nonspecific treatment. In the remaining 3 cases of hypopyon keratitis the sulfapyridine was apparently of no value in preventing the formation of extensive vascularized leukomas.

SUMMARY

A study of the effectiveness of the oral administration of sulfapyridine in the treatment of pneumococcic corneal ulcers is presented. An injection method is described for producing a standard experimental pneumococcic corneal lesion in rabbits. Six series of experimental animals were treated with various amounts of sulfapyridine given by mouth. In the dose employed the drug was found to have little value in controlling established ulcers. To bring out the maximum therapeutic effect, treatment was instituted prior to corneal inoculation in the later series. Large prophylactic doses of sulfapyridine produced a marked reduction in the reaction of the adnexa during the acute phase. In addition, the drug seemed to be somewhat beneficial in controlling the extensiveness of the corneal lesions proper.

Some of the possible causes of the reduced efficiency of sulfapyridine in the chemotherapy of pneumococcic corneal lesions are considered.

Clinical reports are presented of 6 cases of pneumococcic corneal ulcer in which systemic sulfapyridine therapy was employed. In 4 of these the drug was apparently without effect, while in the remaining 2 there may have been some hastening of the convalescence and reduction in the density of the scar.

Dr. Phillips Thygeson provided direction and supervision in the carrying out of the experiments reported. Dr. Karl Meyer and Dr. Richard Thompson assisted with suggestions. Dr. Devorah Locatcher-Khorazo gave practical help in the execution of the problem involved.

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REVIEW OF COLOR VISION

WITH SOME PRACTICAL SUGGESTIONS FOR MEDICAL EXAMINERS

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Most physicians are familiar with the fact that quite a number of men and a few women have defective color vision. Well known also is the fact that the defects are hereditary, as a rule being transmitted through the female and appearing in the male. Beyond this, color vision has no special interest for the physician, as it generally has no direct bearing on the human ailments he is called on to treat. Now, however, many physicians are in the military services, in which color vision is of great importance, and thus they are called on to examine this characteristic of vision. The subject is not well understood, and the numerous errors being made by examiners suggest the need for a review of some of the important facts and possibly some simplification of the present tests.

Persons who are deficient in color vision are nearly always referred to as being "color blind." There never was a more unfortunate term, as it could apply only to those extremely rare persons to whom the environment appears in shades of white and black, very much like an ordinary photographic picture. Usually persons who have color vision defects resent being termed color blind, as they do differentiate at least some colors and they definitely are not blind. Yet how can they know that they are unable to distinguish some colors which their more fortunate neighbors see with ease and certainty? One must realize that each person's concept of his environment is necessarily dependent on his own perceptual and mental equipment. One with a defect of color vision cannot borrow for a moment the visual conception of his normal neighbor for comparison. Thus, the environment of a man, be he either normal or deficient in color vision, appears as he has always seen it because all previous experiences based on his perceptions are the same.

The two conceptions certainly are not alike, though the exact way in which they differ is difficult or impossible to define in mere words. The only way it is possible to get at this elusive phenomenon is by devising various tests which remove any possibility of associating objects with certain colors and remove all criteria of color except color itself. Under these conditions the differences in perception between the normal person

and the person with defective color vision are evident. Misunderstanding and confusion generally arise at this point. It revolves around the failure of all concerned to realize the difference between fact and opinion. To the person with normal color vision it is a clearly established fact that the color vision of the one examined is defective. To the examinee with a color vision defect, it is a matter of opinion that he is deficient in color vision. He believes that he is color ignorant, that he failed to understand what was wanted, that the examiner and also the test were unfair, that he wasn't given enough time, all of which he voices together with many other apparently good reasons. None of them alter the fact; all are rationalizations.

Examiners must also realize that in any representative group of doctors, more than 10 per cent will be defective in color vision. These physicians should never be called on to make decisions regarding color vision. There are two reasons, the obvious one being that they are simply unable to do the tests or to evaluate the results accurately. The other reason is less obvious and because of its insidious nature is not often mentioned or considered. It is nevertheless the most important of all and has to do with the real cause of many of the errors and resultant embarrassment to the Medical Department of the Army. These examiners easily fall into the common error of believing that too much stress is being placed on something which seems to be of no practical importance.

The history of color vision testing is replete with numerous attempts to develop a test which would be accurate beyond question and practical to use and which would classify the type of color vision defect. No test has yet proved entirely reliable or generally acceptable. There are several theories of color vision, none being universally accepted. Much confusion is added by the different terms used in the various classifications of color vision deficiency, each based on its own theory. In those instances in which the terms are the same, they often have different interpretations.

THE SENSATION OF COLOR

Sensation of color has three variables. It varies as to hue, which depends on the wavelength of the light rays falling on the retina. It varies as to saturation or purity, depending on the range of wavelengths of light falling on the retina; if a color is mixed with white, it is said to be less saturated, and the amount of saturation is dependent on the total percentage of color in the mixture. It also varies as to luminosity, which depends mostly on the intensity of the stimulus or the amount of light energy falling on the retina.

The laws of color mixtures are stated briefly as follows: Any color can be produced by mixing not more than three of the primary spectral

colors provided one adds white or black as necessary for the proper saturation. The primary spectral colors, according to Young and Helmholtz, are red, green and blue. None of the three can be produced by either of the other two. They also form the basis of Maxwell's color triangle.

CLASSIFICATION OF COLOR VISION DEFECTS BASED ON THE YOUNG-HELMHOLTZ THEORY

The basis of the Young-Helmholtz theory of color vision is this: It postulates that there are three different kinds of cones, not histologically distinguishable, which when stimulated by a continuous spectrum give rise to the sensation of either red, green or blue. Each cone is stimulated to some extent by the entire visible spectrum but especially by a certain portion of it. The sensation of any color can be produced by the stimulation of one or more of these cones, or if all are stimulated equally, the sensation of white is produced. It is apparent that there is a psychologic factor involved as well as a purely physiologic one. This is because the stimuli arising from the three kinds of cones are blended centrally, and this gives rise to the sensation of the color perceived.

The classification of color vision on the basis of the Young-Helmholtz theory is shown here in outline. It refers only to the congenital type of color defect and not to the acquired type, which is nearly always associated with more or less severe toxic symptoms.

1. Trichromatic vision. The trichromat perceives all the spectral colors which can be made up by suitable combinations of the three primary colors (with or without white or black added). This is normal color vision.

In anomalous trichromatic vision the relative quality of the sensation of the three primary colors differs from the normal in that there may be merely a relative inability to appreciate red (partial protanopia or green sightedness) or green (partial deuteranopia or red sightedness).

2. Dichromatic vision. The color sensations of the dichromat are based on the perception of only two colors. The sensation of one of the three primary colors perceived by the normal person is absent. If red is absent, the condition is called protanopia; if green, it is called deuteranopia, and if blue is absent, it is called tritanopia.

3. Monochromatic vision. No color differentiations are made. This is extremely rare and few cases have been reported.

The anomalous trichromats have no characteristic defects except in the relative difficulty with which they make color discriminations. They usually perceive fully saturated colors of high luminosity, but with uncertainty. They are the ones who after much time and evident indecision generally "guess" correctly. Examiners often think of this group as "not dangerously color blind" or "color ignorant." It should be

pointed out that examinees falling into this group by no means always "guess" correctly in conditions simulating military operations.

To the red-blind subject the red and the bluish green part of the spectrum are uncolored. He does not perceive or experience these color sensations at all, and the red end of this spectrum is simply grayish. On one side of the blue-green portion of the spectrum, which is also dark or grayish, he sees yellow and on the other side blue.

To the green-blind person the green part of the spectrum is uncolored or grayish. On one side he perceives yellow and on the other side blue.

The red-blind and the green-blind persons see only the yellow and the blue and do not perceive any other colors. The reds and the greens thus look alike, and there also seems to be an unusual brightness of the yellows and the blues as compared with the reds and the greens. This is extremely important in some tests for color vision, such as the Ishihara. Any selection of red or green objects is on the basis of association or on the basis of the light value of the object itself and is therefore largely accidental.

THE ISHIHARA TEST

Perhaps the most reliable test for demonstrating the conditions just cited is that which makes use of the Ishihara book of plates. Reference to the explanatory notes accompanying the book makes the classification of the defect fairly easy. However, this test is not a simple one, and several precautions must be observed. It must be performed in good daylight and not in artificial illumination. This is an extremely important fact often overlooked. The book should be at a distance of 20 to 30 inches (50.5 to 76 cm.) from the eyes, with the plane of the plates at approximately right angles to the line of vision.

Unfortunately, these plates are now readily available in public libraries and have even appeared together with explanatory notes in popular magazines with national circulation. Nearly all examinees know that this is a commonly used test in the military services, especially in the flying corps, and they naturally can be expected to study these plates. The diagnostic value of the plates is therefore much less than could otherwise be expected.

The alert normal person will correctly read the plates, shown in an irregular manner, at the rate of least one every one or two seconds. Examinees requiring a longer time are either anomalous trichromats, dichromats who have thoroughly memorized the test and require a little time to think of the correct answer or persons with some degree of psychomotor retardation. The last type is uncommon. Therefore, these slow examinees are usually deficient in their color vision, and allowing more time for such examinees to read plates causes mistakes in selection.

CLASSIFICATION OF COLOR VISION DEFECTS BASED ON THE EDRIDGE GREEN THEORY

The other classification of color vision commonly used so far as the Army is concerned is based on the Edridge Green theory of color perception. Lieut. Col. E. E. Cooley and Lieut. Col. M. Grow [1] stressed the usefulness of this classification in the interpretation of the Holmgren yarn test. It is easy to understand, and while some of the terms are like those in the Young-Helmholtz classification, they have somewhat different meanings. It is extremely important not to confuse the definitions of the terms in respect to the two theories.

This classification also applies only to congenital defects of color vision. Edridge Green assumed that primitive life forms had only a light sense and that color sense was a later evolutionary development. As evolutionary development continued in mammals and especially in primates, more and more spectral colors were recognized. In the human range, the normal individual recognizes the following six spectral colors: red, orange, yellow, green, blue and violet. Persons whose color vision is defective are classified on the number of spectral colors perceived. Each spectral color is called a psychophysical unit.

1. Monochromatism. Here the spectrum appears only as shades of gray. The condition is very rare and corresponds to the monochromatic vision in the Young-Helmholtz classification.

2. Dichromatism. Here the spectrum appears as shades of gray except that red is perceived at one end and blue-violet at the other. This corresponds closely with the dichromatic vision in the Young-Helmholtz classification. The characteristic errors made by this group are the red-green confusions.

3. Trichomatism. Here the three spectral colors seen are red, green and violet. Orange, yellow and blue are not seen as distinct colors. The characteristic error of this group on the Holmgren yarn test is that they confuse green with brown.

4. Tetrachromatism. Here the four spectral colors seen are red, yellow, green and violet. Blue is not seen as a separate color but appears as a shade of green. The characteristic error of this group on the Holmgren test is that of confusing green with blue and blue-green.

5. Pentachromatism. Here the five colors seen are red, yellow, green, blue and violet. Orange is not seen as a definite color. The characteristic error of this group is to confuse red and orange.

6. Hexachromatism. This is the state of the normal person, who sees the six spectral colors, red, orange, yellow, green, blue and violet. He will pass all of the color tests with ease and certainty.

7. Heptachromatism. This is a rare condition. It consists of the ability to recognize, in addition to the six spectral colors ordinarily seen, a seventh between the blue and the violet, called indigo. Another important fact is that the entire

1. Cooley, E. E., and Grow, M.: Color Vision, Army M. Bull., 1936, no. 34. Cooley, E. E.: The Examination of Color Perception, ibid., 1937, no. 38.

spectrum is brighter and color differentiations are made with greater facility than normal. The subjects pass all the usual color tests with great ease.

8. In addition to the aforementioned defects in the number of colors perceived, so-called neutral or uncolored bands may be present in certain portions of the spectrum. This is most common on the red end of the spectrum, where the darker reds blend into gray or black before this takes place with normal vision. This is spoken of as a shortened red end of the spectrum. The characteristic error on the Holmgren test is the confusion of gray with red. On the Williams lantern test, there is a failure to see a dark, fully saturated red of low luminosity which is seen by the person with normal color vision. This shortening of the spectrum takes place also in the violet end. In other portions of the spectrum, the defect is brought out by confusion of gray with the color involved, such as gray with green if the neutral band is in the green portion of the spectrum.

OTHER THEORIES

The many other theories of color vision will not be referred to here. This is not because they may not be equally valid but simply because they have no bearing on the immediate problem. One is referred to the excellent discussion of the subject by Duke-Elder,[2] who gives numerous references, and likewise to the work of Lieut. Col. E. E. Cooley and Lieut. Col. M. Grow.[1]

AN EVALUATION OF THE HOLMGREN YARN TEST, CORRECTLY PERFORMED

The Holmgren yarn test is definitely not a simple test as is generally assumed. As performed by many examiners, it is a waste of time and serves only to rationalize the examinee's mistake. This test when properly done takes from fifteen minutes to a half hour or more. The technic is difficult to teach, and the proper interpretation of the results requires a normal examiner with considerable experience. In about three fourths of the cases, even when it is carefully done on a person suspected of having defective color vision, the test does not give a rational basis on which the conscientious examiner can base a decision as to whether the examinee is to be qualified or not.

There are a number of essentially similar technics for the performance of the Holmgren yarn test. One of these is outlined here:

From one hundred to two hundred skeins of yarn are required, which include a sufficient number of confusing shades, such as rose, blue, blue-green, gray, brown, violet, orange and light shades of greens and reds. They should be spread out on a gray or a white background in good daylight but not sunlight. They must be kept clean and must be protected from the light when not in use to prevent fading of the colors.

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2. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1932, vol. 1.

The examinee is first asked if he knows what the true colors are, and if he is uncertain, which is almost invariably the case, the names of the six spectral colors are mentioned.

Next, the difference between colors, their degrees of saturation, and mixtures is made clear to the examinee. For the sake of simplicity, the various degrees of saturation are referred to as shades. It is essential that this matter of differences should be understood, as neither the examiner nor the examinee can get far if the same facts are not understood by both. For achieving this, a series of blue skeins is excellent. One selects a fully saturated one, an intermediate shade and an extremely light shade. Needless to say, these skeins of yarn must be carefully selected as to color so that mixtures are not included. The examiner points to the skeins and says, "Here we have an example of shades of a given color. The name of this color will not be mentioned as it is apparent to you." He then points to the darkest one and says "If this were paint, one would get this next lighter shade by adding white. If still more white is added, in this case a lot more, this very light shade would be obtained. Now, if I held up this intermediate shade and asked you to select from the large pile of yarns all skeins that were this color, you should select among others this very light shade as well as this very dark shade, as they are, of course, merely shades of the same color I hold in my hand."

The three shades are then put down in order on the table and a pink is placed next to the light blue.

The examiner says, "We now have a light shade of another color. If we could mix these, we would get a color something like this." He now picks up a rose-colored yarn and places it so that one end is on the pink and the other on the light blue. He says, "This, then, is called a mixture because it contains both of these colors, as you see by direct comparison." It is extremely important that the examinee clearly understands the difference between colors, their saturations or shade, and mixtures. Unless he does, the test is practically worthless.

Next, a large envelop is given the examinee, and the examiner selects a saturated or dark red. This is important, as persons with a shortened red end of the spectrum will confuse red with gray. He tells the examinee to place in the envelop all skeins of yarn in the large stack that are the same color as this test skein. This should include all of the light as well as the darker shades. "If you place in the envelop a skein of yarn which is a mixture of the color of the test skein with another color, it is counted as an error." In order that the test may be accurate, it should also be pointed out that if a skein of yarn the color of the test skein, either a lighter or a darker shade unmixed with another color, is left in the stack, this also is to be counted as an error. This caution prevents leaving all doubtful skeins in the larger stack.

It is suggested to the examinee that he take the skeins one by one, as he comes to them, and place them either in the envelop or in a discard stack.

The test skein should be held at about eye level, as this measure gives the examiner an index of how certain the examinee is. The normal subject will give the test skein a glance and not refer to it again as a rule. The subject with defective color vision will often glance at the test skein for each skein selected. The test is repeated with the very dark green. If no red and rose confusions are made at first when the red skein is used, then a rose yarn is also used for a test skein. It should be unnecessary to add that all the skeins must be well

mixed together between each test. Those selected should never be put aside and thus out of the test stack of skeins.

The color confusions should be noted, such as red with rose; green with blue, or green with brown, and so on, and the Edridge Green classification is then made on the characteristic confusions made. Confusion of a test color with gray indicates a neutral or uncolored band in that spectral range.

This is a far different story from the usual one of the examiner selecting, for instance, a bright red and asking the examinee to say what the color is and to select a skein or two the same color, and so on. Generally, if an error is made under that casual method of testing, it is discounted as a "natural mistake" or one due to "color ignorance" and the candidate passed as normal because further investigation is too time consuming and many more are to be examined before the end of the day.

In examining flying cadet applicants, the Ishihara test or a test using Ishihara plates like the New American Optical Company Book is used, and if no errors are made, the candidate is considered normal. If errors are made, the plate numbers are noted on the examination form. Next, the Holmgren yarn test is performed and the result recorded. Then a decision must be made by the examiner as to whether the examinee is qualified or not. Does he have an adequate basis on which he can make a reasonable decision?

If the examinee made red-green confusions on the Holmgren test, he would, of course, have to be disqualified. If he made green-brown confusions (trichromatism, Edridge Green), green-blue or blue-green confusions (tetrachromatism, Edridge Green) or red-orange confusions (pentachromatism, Edridge Green), should he be qualified or not? One cannot be certain whether or not the examinee is "dangerously color blind." If he is not, presumably a great injustice is done both the examinee and the government if he is disqualified. If he is qualified and is "dangerously color blind," mistaken perception of the color of flares, signal lights, colors on wires, shades of colors on a map, and so on, can easily lead to disaster involving the lives of many innocent persons as well as destruction of valuable equipment.

The present regulations as written are not very clear on this point, as they state:[3]

"Impairment of the sense of color perception in a pronounced degree is cause for rejection. The minimum requirement for general qualification should consist of the ability to distinguish and identify without confusion the color of an object, substance, material or light that is uni-

3. Standards of Physical Examination for Entrance into Regular Army, National Guard and Organized Reserves, Army Regulations 40-105, Changes 5, United States Army, Medical Department, 1940, paragraph 18 C, for Candidates for Commission.

formly colored pure red, and the color of an object, substance, material or light that is uniformly colored pure green."

The obvious question is, first, what constitutes "a pronounced degree of impairment of color perception?" And, second, just how literally should one interpret the sentence regarding the identifying "without confusion the color of an object, substance, material or light" that is pure red, and likewise for green? One cannot help but wonder if the writer of the regulations realized how severe this test is.

A study recently completed in the department of ophthalmology at the School of Aviation Medicine indicates that our present system is not altogether satisfactory. It is generally thought that persons who can pass the Ishihara test can be considered normal. The percentage of errors is undoubtedly extremely low if the test is given as described. When the Holmgren test is given properly as a "confirmatory test," only about 8 per cent will make red-green errors. These must be disqualified. Thus, roughly 92 per cent of those who show evidence of color vision deficiency by their inability to pass the Ishihara test cannot be disqualified or qualified for appointments or commissions except on the interpretation the medical examiner wishes to place on his Holmgren findings. It is therefore altogether a matter of the examiner's opinion. It will depend on many factors, the main ones being how much he knows about color vision testing and the interpretation of the tests, whether he is himself deficient in color vision, and whether he interprets the regulations literally or not.

Should the examinee who selects a brown or a blue, for example, to add to his greens or a rose to add to his reds be disqualified on the strict interpretation of the regulations which is presumed in the phrase "identify without confusion"? To many this may appear as only an academic point, but even on the loosest possible interpretation of the regulations, the selection of a rose as belonging with the reds or of a blue or a brown as belonging with the greens, are matters of fact, which no amount of rationalization can alter. The vast majority of examinees who make errors on Ishihara plates will actually make one and usually more of these errors, and thus should either receive a waiver on their color vision or be disqualified. Often the whole matter is disposed of by the insertion of the word "Normal" in the line for color vision.

This study was carried out on a series of 50 subjects who made errors on Ishihara plates at the School of Aviation Medicine. The figures for nearly again this number were essentially the same. These examinees were given a careful Holmgren test essentially as described by Major J. M. Hargreaves in United States Army Technical Manual 300, which required between twenty minutes and over one-half hour in almost every case. They were then classified on the Edridge Green

classification. They were also given a Williams lantern test with the technic described in the following paragraph:

> From 1 to 6 candidates were seated near the end of a 20 foot (6 meter) dark room. Each was given a large writing pad and pencil and told to write his name, the date and "Series One" at the top of the page. They were given at least fifteen minutes' dark adaptation. If this procedure is questioned, let it be pointed out that much of the flying in modern war is at night, and, of course, night time is the only time when many flares are used by ground and air troops. Therefore, it is reasonable to allow for dark adaptation. A small 7½ watt light was turned on well above and behind the examinees. This gave light enough for writing but not enough to disturb the test. Then the Williams lantern was turned on, and the examinees given the following instructions: "You are to see a series of lights. Before each one, you will be given its number, which you will write on the left side of the page, after which you will write the name of the light. It is unnecessary to qualify it as being light or dark, merely name the color." The one-sixteenth inch aperture was used first without a filter. The eighteen colors on the disk were then shown consecutively, five seconds being allowed for each one. They are not numbered consecutively on the disk, and a different starting point was taken each time. The examinees were then instructed to turn the page over and write on the top of the back "Series Two." This time the smoke filter simulating the effect of fog, smoke, distance haze and other factors was interposed and the procedure repeated. The papers were collected and immediately corrected on the basis of a "key" furnished with the instrument.

The color vision of the examiner plays no part in such a procedure. The test is rapid and simple, requires little or no experience, and can be done by an intelligent, trained enlisted man, though the papers should be corrected by an officer. Best of all, a definite answer to the question can be had on the basis of a record in the examinee's own handwriting compared with a key.

The following criteria based on the regulations were used as disqualifying errors:

Calling white green or green white, calling red white or white red or calling green red or red green.

The importance of these mistakes in combat is apparent to any one. Making any one of them is, therefore, entirely and reasonably a cause for disqualification. There is no need for rechecks, as, obviously, one mistake is enough. There is in the examiner's hand incontrovertible evidence on which he can make a reasonable decision, not just base an opinion.

It was found that a number of normal persons would call green blue or blue green; some also would call a rose color light red, or a light through a cobalt blue glass either red or blue. These errors were not considered significant. Some persons who made errors on Ishihara plates called amber or orange green and should be disqualified. Calling violet or lavender red was not considered disqualifying if this was the only error, as an occasional normal examinee would do this.

This study shows clearly that of all those who made errors on Ishihara plates, those who made red-green errors on the Holmgren, or 8 per cent of the entire group, made similar errors on the Williams lantern test. They were the dichromats on the Edridge Green and also on the Young-Helmholtz classification. Those who confused browns with greens on the Holmgren (trichomats, Edridge Green) all made disqualifying errors on the Williams lantern test. The trichromats constituted 16 per cent of the entire group. Combining those two, one has 24 per cent or about one fourth.

Thus, on the basis of the Ishihara examination followed by the Holmgren test as confirmatory, about one fourth of those who make errors on Ishihara plates could be disqualified on the Holmgren test, according to the results in the Williams lantern test. This leaves 76 per cent or about three fourths of those who make errors on the Ishihara plates for whom the Holmgren test gives no reasonable basis on which the examiner can conscientiously make a decision, even when the proper technic is carefully followed. This is regrettable when one considers that twenty minutes and often more than a half hour is spent on each subject. The Holmgren test showed that 68 per cent of the entire group were tetrachromats (Edridge Green) and 8 per cent were pentachromats (Edridge Green). Thus, all who failed on the Ishihara plates showed evidence of some color vision deficiency. It should be pointed out that care was taken to see that whatever errors the examinees made on the plates were not due to carelessness.

Testing these tetrachromats with the Williams lantern showed that three fourths of them made significant errors. One half of the pentachromats also made significant errors on the Williams lantern test. This furnishes clear evidence that the Holmgren test, even when carefully done, which is very rarely the case, does not give evidence justifying the time spent. One cannot qualify or disqualify candidates wholly on the basis of the Edridge Green classification except when red-green confusions are made as in dichromatism.

Of the entire group making errors on the Ishihara plates, 20 per cent when subsequently tested by the Holmgren yarns and the Williams lantern did not make significant errors on the latter test and were accordingly qualified; 80 per cent made errors as described previously and were disqualified.

This also clearly indicates that the point of view, commonly held by flight surgeons, that the Ishihara test did not require any confirmatory test cannot altogether be upheld. Two facts must be kept in mind, however, in this connection. The total number of those persons in the aggregate is not very large. One must not assume that they do not have a color vision defect. The errors made on the Ishihara plates, the errors made on the Holmgren yarns and those errors not considered

disqualifying made on the Williams lantern test, all point definitely to the contrary. One can only be reasonably sure that the statistical likelihood of their making errors is small. In other words, they may be said to be "not dangerously color blind," to use a common, though somewhat unfortunate, term. No one knows whether or not under conditions of excitement or stress they may make serious errors.

SUMMARY

A brief review of the Young-Helmholtz and Edridge Green theories and classifications of color vision defects is presented.

A correct but not original technic for the Holmgren yarn test is presented.

A technic for the Williams lantern test is suggested, simulating conditions of military operations more closely than other tests of color vision.

The suggestion is made that the time-consuming Holmgren yarn test be omitted together with the Edridge Green classification of color vision defects based on the color confusions recorded in this test. This suggestion is based on the results of a study made at the School of Aviation Medicine indicating quite clearly that about three fourths of the examinees who made mistakes on the Ishihara plates could not be qualified or disqualified on the results of the Holmgren yarn test used as a "confirmatory test" for the Ishihara test.

From the same study it was apparent that the idea commonly held by flight surgeons that the Ishihara test does not require any confirmatory test could not be entirely substantiated. This is based on the fact that 20 per cent of those who make mistakes on the Ishihara test do not make significant errors on the Williams lantern test and therefore could be qualified. For all practical purposes it is reasonable to assume that they will not make mistakes under ordinary circumstances.

It is recommended that the Williams lantern test be used in place of the Holmgren yarn test as a confirmatory test since it is simpler, several examinees can be tested at once, and, with the technic outlined, a written record is available which can be compared with the key. The examiner's color vision does not complicate the picture.

A simplified modification of the Williams lantern has been submitted to higher authority for consideration.

INCLUSION OF SCLERA IN CORNEAL TRANSPLANTATION

A GROSS AND MICROSCOPIC STUDY

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The technical aspects of transplantation of the cornea have been the subject of numerous investigators for more than one hundred years. Not until von Hippel,[1] Elschnig,[2] and, more recently, Filatov,[3] Thomas [4] and Castroviejo [5] were the manifold difficulties largely surmounted. How-

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1. von Hippel, A.: Eine neue Methode der Hornhauttransplantation, Arch. f. Ophth. (pt. 1) **34**:108, 1888.

2. Elschnig, A.: Ueber Keratoplastik, Ber. ü. d. Versamml. d. deutsch. ophth. Gesellsch. **42**:331, 1920.

3. Filatov, V. P.: Zur Technik der partiellen durchgreifenden Keratoplastik, Ztschr. f. Aughenh. **65**:147, 1928; Transplantation of the Cornea, Arch. Ophth. **13**:321 (March) 1935.

4. Thomas, J. W. T.: (*a*) Transplantation of the Cornea: A Preliminary Report of a Series of Experiments on Rabbits, Together with a Demonstration of Four Rabbits with Clear Corneal Grafts, Tr. Ophth. Soc. U. Kingdom **50**: 127, 1930; (*b*) Successful Grafting of the Cornea in Rabbits, Lancet **1**:335, 1931; (*c*) Transplantation of Scleral Tissue on to Rabbit's Cornea, Tr. Ophth. Soc. U. Kingdom **52**:64, 1932; (*d*) Observations on Some Matters Associated with Experimental Corneal Grafting, Brit. J. Ophth. **18**:129, 1934; (*e*) The Technique of Corneal Transplantation as Applied in a Series of Cases, Tr. Ophth. Soc. U. Kingdom **55**:373, 1935; (*f*) Experimental Heterogenous Corneal Grafts, ibid. **56**:97, 1936; (*g*) The Clinical and Microscopic Appearances of Experimental Grafts of Scleral Tissue on to Rabbits' Corneae, ibid. (pt. 1) **57**:198, 1937; (*h*) The Results of Corneal Transplantation, Brit. M. J. **1**:114, 1937; (*i*) The Technique of Corneal Transplantation with Recent Modifications, Tr. Ophth. Soc. U. Kingdom (pt. 2, 1937) **57**:520, 1938.

5. Castroviejo, R.: (*a*) Keratoplasty: An Historical and Experimental Study, Including a New Method, Am. J. Ophth. **15**:825 and 905, 1932; (*b*) Keratoplasty:

(Footnote continued on next page)

ever, as the surgical procedure now will result in success in the majority of cases when employed by trained operators, the demand for corneal material with which to provide transparent cornea far exceeds the cornea available.

In certain European countries, notably Russia, where blindness is prevalent, the source of corneal tissue is more abundant in that the laws of the country allow use of cadaver eyes. However, in America social legislation has not as yet permitted this rich reservoir to be tapped, and in spite of valiant efforts toward this goal, ophthalmic surgeons still are dependent for corneal tissue on eyes which have been enucleated because of a pathologic process, usually malignant growth in the posterior segment, and on eyes from stillborn infants.

Because of the unequal ratio between supply and demand, ophthalmic surgeons generally obtain several small squares from one cornea. The usual window transplanted is 4 mm. square. In the normal cornea three such squares can be obtained without difficulty, but in cutting the fourth square the operator may remove an extremely small tag of limbus or scleral tissue. Castroviejo has made this observation clinically and, being confronted with the situation, has proceeded to transplant the fourth square with the small tag of sclera attached. The square always grafted well, barring untoward occurrences, but the operation was invariably complicated by a more severe reaction than that accompanying transplantation of the other three squares. Castroviejo has observed that the eye with the extremely small tag of sclera in the transplanted cornea showed a greater conjunctival reaction and that vascularization of the corneal transplant was more prone to occur. In addition, the cornea in the vicinity of the sclera, both in the host and in the graft, became slightly opaque in time. Later the sclera gradually disappeared, leaving a permanent scar in its place. As a result, such grafts were not considered as successful as those which contained no sclera. For these reasons it was considered desirable to investigate the processes in a series of rabbits receiving corneal grafts along one margin of which a portion of sclera was attached.

Report of Seven Cases, ibid. **17**:932, 1934; (*c*) Keratoplasty: Report of Cases with Special Reference to Complicated Ones, J. M. Soc. New Jersey **32**:80, 1935; (*d*) Modern Aspects of Corneal Transplantation, graduate lecture given before the American Academy of Ophthalmology and Oto-Laryngology, 1936; (*e*) Keratoplasty: Microscopic Study of the Corneal Grafts, Tr. Am. Ophth. Soc. **35**:355, 1937; (*f*) Present Status of Keratoplasty, Arch. Ophth. **22**:114 (July) 1939; (*g*) Keratoplasty: Comments on the Technique of Corneal Transplantation, Sources and Preservation of Donor's Material, Report of New Instruments, Am. J. Ophth. **24**:1 and 139, 1941.

REVIEW OF THE LITERATURE

The first experimental work on corneal transplantation was performed by Reisinger [6] in 1824. Power [7] in 1872 reported his fundamental observations on the microscopic examination of corneal transplants. Since that date an enormous literature has grown up around the subject.

The contributors to the clinical aspects of corneal transplantation are legion. The more outstanding are von Hippel,[1] Sellerbeck,[8] Zirm,[9] Löhlein,[10] Elschnig,[2] Leoz-Ortín,[11] Filatov,[3] Thomas [4] and Castroviejo.[5] Among the pioneers and contemporary investigators of the microscopic study of corneal grafts have been Dürr,[12] Wagenmann,[13] Fick,[14] de Lieto Vollaro,[15] Salzer,[16] Fuchs,[17] Löhlein,[10] Magitot,[18] Bonnefon and Lacoste,[19] Leoz-Ortín,[11] Ascher,[20] Sommer,[21] Frieberg,[22] Castroviejo [5] and Thomas.[4]

In 1932 Thomas [4c] reported his preliminary observations on scleral grafts applied to the corneas of rabbits. In his experiments a circular graft of the whole thickness of the sclera alone was transplanted into the

6. Reisinger, cited by Nance, W. O., in Wood, C. A.: A System of Ophthalmic Operations, Chicago, Cleveland Press, 1911, vol. 2, p. 1013.

7. Power, H.: On Transplantation of the Cornea, Rep. Internat. Ophth. Cong. **4**:172, 1872.

8. Sellerbeck: Ueber Keratoplastik, Arch. f. Ophth. **24**:321, 1878.

9. Zirm, E.: Eine erfolgreiche totale Keratoplastik, Arch. f. Ophth. **64**:580, 1906.

10. Löhlein, W.: Fortschritte auf dem Gebiete der Hornhauttransplantation, Ber. ü. d. Versamml. d. deutsch. ophth. Gesellsch. **52**:72, 1938.

11. Leoz Ortín, G., cited by Castroviejo.[5e]

12. Dürr, E.: Ueber die Erfolge der keratoplastischen Versuche, Klin. Monatsbl. f. Augenh. **17**:317, 1879.

13. Wagenmann, A.: Experimentelle Untersuchungen zur Frage der Keratoplastik, Arch. f. Ophth. **34**:211, 1888.

14. Fick, A. E., cited by Castroviejo.[5e]

15. de Lieto Vollaro, A., cited by Castroviejo.[5e]

16. Salzer, F.: Beiträge zur Keratoplastik: zur Biologie der Hornhautverpflanzung, Arch. f. Augenh. **110**:450, 1937.

17. Fuchs, E.: Zur Keratoplastik, Ztschr. f. Augenh. **5**:1, 1901.

18. Magitot, A.: Recherches expérimentales sur la survie possible de la cornée conservée en dehors de l'organisme et sur la kératoplastie différée, Ann. d'ocul. **146**:1, 1911; Transplantation of the Human Cornea Previously Preserved in an Antiseptic Fluid, J. A. M. A. **59**:18 (July 6) 1912.

19. Bonnefon, G., and Lacoste, A.: Recherches histologiques sur la greffe cornéenne autoplastique, Arch. d'opht. **33**:206, 267 and 326, 1913.

20. Ascher, K. W.: Zur Histologie der Keratoplastik, Ber. ü. d. Versamml. d. deutsch. ophth. Gesellsch. **43**:198, 1922; Zur Keratoplastikfrage; Histologische Untersuchungen an menschlichen Keratoplastikmaterial, Arch. f. Ophth. **111**:446, 1923.

21. Sommer, I.: Zur Histologie der Keratoplastik, Arch. f. Ophth. **115**:620, 1924.

22. Frieberg, T.: Erfahrungen über optische Keratoplastik beim Menschen, Acta ophth. **5**:122, 1927.

cornea. He stated the belief that it was possible successfully to transplant scleral tissue to replace the whole thickness of the cornea without vascularization's taking place. However, in 1937 he noted further that vascularization of the cornea did occur in the majority of the scleral transplants. Thomas concluded that a moderate degree of vascularity accelerates the transition from a white scleral graft to a partly transparent graft.

All the other workers have confined their investigations to transplanting clear cornea by the following methods: total transplantation of the cornea, superficial lamellar transplantation and partial penetrating corneal transplantation. A search of the literature does not reveal a previous experimental study of the inclusion of sclera and cornea in the transplant.

EXPERIMENTAL METHODS

Healthy white rabbits about 3 months of age and weighing 3 to 4 pounds (1.3 to 1.8 Kg.) were used for reasons of standardization. The progress of each transplant, its success or its failure, was noted. At determined intervals the eyes were enucleated and histologic sections were prepared for a microscopic study.

Anesthesia.—General anesthesia was obtained by the use of pernostonsodium (sodium secondary butylbetabromallylmalonylurea) injected with a hypodermic needle subcutaneously. The skin of the belly wall was chosen for the injection. It was found that 1 to 1.25 cc. of the drug was sufficient to produce adequate narcosis within one-half hour. In larger animals 1.5 cc. was administered. Occasionally the dose proved too high or the tolerance of the rabbit was decreased, with the result that the animal succumbed shortly after the injection. In most instances the general anesthesia was supplemented by topical anesthesia induced with 0.5 per cent pontocaine hydrochloride, which was instilled into the eye during the operation.

Preparation of the Eye of the Host.—The pupil of the eye was dilated with 3 per cent atropine sulfate instilled every ten minutes for one hour before the operation. In addition, a subconjunctival injection of a preparation of 4 per cent cocaine hydrochloride (2 minims), 1,000 epinephrine hydrochloride (1 minim) and 3 per cent atropine sulfate (1 minim) was injected subconjunctivally above and below the limbus. Some danger always resulted from the injection of cocaine hydrochloride and epinephrine hydrochloride, and in 1 case it was felt that the resulting sensitization of the nerve endings was responsible for the death of the rabbit during the operation. However, if the dose mentioned was adhered to, the animal generally tolerated the injection well.

Immobilization of Rabbit.—The operator performed all the operations sitting, and one assistant was always required. An unsterile "scrub nurse," in addition, was of great help in procuring material during the actual operation when the hands of both the operator and his assistant were sterile.

A specially constructed hold for the head of the rabbit, devised by Castroviejo, was utilized (fig. 1). This consisted of a rubber-covered mouth piece with two arms, one to lie over the nose and the other to lie under the jaw. A screw device immobilized the apparatus, and, at the same time, the animal's head and mouth were not injured. A system of three joints allowed the animal's back, neck and head to be in the proper position for adequate breathing, and yet the head could not move from the table. The whole machine was riveted to the metal table top. A small towel then was wrapped around the belly of the animal and tied with cord

to the edge of the table. Both the forelegs and the hindlegs were extended and immobilized on the table with stout cord.

The vibrissae of the rabbit and the more prominent hairs about the eye were clipped off with the scissors. No attempt was made to remove all hair in the vicinity of the eye for aseptic reasons.

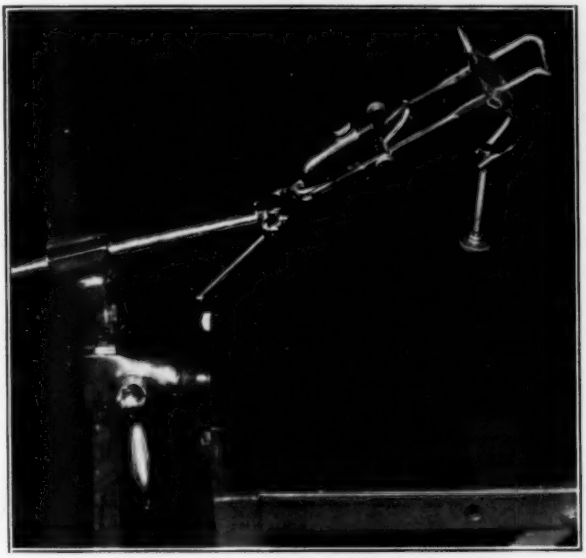

Fig. 1.—Apparatus to hold the head of the rabbit during corneal transplantation.

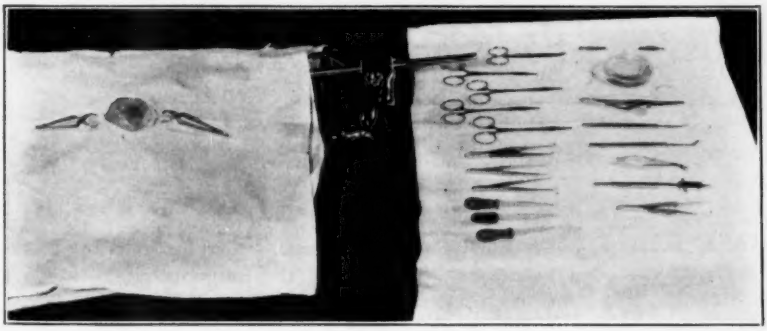

Fig. 2.—The rabbit draped for corneal transplantation.

Surgical Procedure.—At this point the operator and the assistant scrubbed their hands with soap and water for five minutes and after rinsing them with alcohol painted the eyelids of the rabbit with 3 per cent iodine. A small hole was punched in gauze saturated with 70 per cent alcohol, and the gauze was placed over the eye. The entire rabbit was covered with a sterile drape in which a hole was present for the eye. The drape was clamped in position and the surgical table moved into position (fig. 2).

Twenty per cent solution of mild protein silver was instilled and then a 1 : 1,000 epinephrine and a 0.5 per cent pontocaine solution. Separation of the eyelids was maintained with a small mosquito forceps. The double-bladed knife devised by Castroviejo was used to outline a 4 mm. square in the center of the cornea. Immobilization of the eye was obtained best by the use at one time of two fixation forceps over the insertion of two rectus muscles. The assistant operator was required to fix the eye with one of the forceps while the operator applied fixation opposite the double-bladed knife. Moderate pressure was applied to the cornea with the double-bladed knife when the square was being outlined so that approximately one half to two thirds of the outer layers were incised.

It requires considerable care and practice to place the suture so that it covers the four corners and the four centers. At the beginning, lack of the necessary

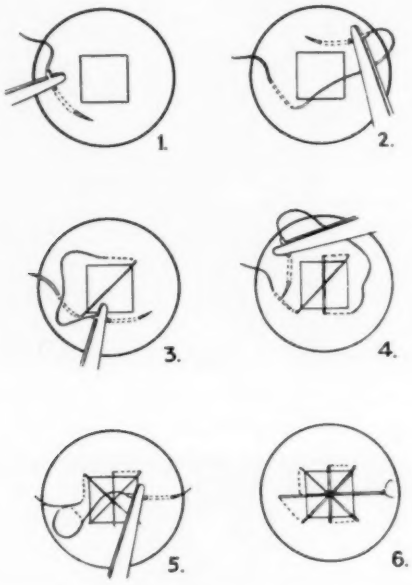

Fig. 3.—Corneal transplant suture devised by Castroviejo.

technical skill often resulted in misplacement. The suture varied from being too superficial, and thus working out too soon, to perforating the anterior chamber. In the latter case, insertion of the remainder of the suture became considerably more difficult. In all the transplantations the continuous corneal suture described by Castroviejo was used, and it was placed 1 to 1.5 mm. outside the edges of the outlined square (fig. 3). At first the square was clearly enough outlined without the use of 2 per cent fluorescein, but as the operation proceeded the markings usually became more indistinct, and the fluorescein was then instilled.

It was found that the suture could be more easily inserted if the operator applied fixation at the limbus in a line with the direction of the needle. At the same time the assistant applied fixation at the limbus 90 degrees from the direction of the needle. Experience further showed that the operator could insert the needle into the stroma of the cornea with greater facility if he grasped it with the needle holder just anterior to the center of the curve and then followed the curve in placing the suture.

Another suture was placed by a single bite in the center of the outlined square to facilitate the removal of the segment at a later stage.

The suture material and the needle devised by Castroviejo are ideal for transplantation, but these are not always available for animal work, and in their place a fine black 6-0 or 8-0 suture thread with a small 14 mm. Kalt noncutting needle sufficed.

After the suture was placed the operator drew it tight to make sure that the corners and centers were all covered and then withdrew it a short way, beginning at its distal end. The loops were laid conveniently around the square and their positions noted well to allow for rapid drawing up at the completion of the operation.

In the early experiments the square from the host was removed at this stage. However, because of the formation of fibrin from the aqueous humor and resulting matting of the sutures, in the later operations the square of the donor was removed first and set aside.

Preparation of Donor Eye.—The cornea to be used in the transplant was obtained from the eye of another rabbit. As a rule the animal to be killed had been operated on previously in the other eye, and this eye was ready for microscopic study.

Fig. 4.—Cross section of a rabbit eye, showing the site for removal of a corneoscleral graft (× 150).

The donor eye was enucleated and as much of the conjunctiva cleared away from the limbus as possible. Absolute sterility of the donor eye is, of course, difficult to obtain. However, if the eye was washed well under tap water and placed in three successive changes of sterile physiologic solution of sodium chloride at room temperature, the cornea could then be transplanted. The enucleated eye was wrapped in moist sterile gauze with the cornea exposed and held between the ends of the fingers of the left hand. The 4 mm. square could then be outlined. The square was placed at the limbal region to include 3 mm. of cornea and 1 mm. of sclera (fig. 4).

From one half to two thirds of the outer layers were incised without beveling. Two per cent fluorescein was dropped onto the cornea to make the incisions more visible. One of the corneal edges of the outlined square was cut through with a special keratome 4 mm. wide and held at an angle of about 20 degrees from the vertical in order to obtain shelving of the inner layers of the cornea. The keratome was placed so that one side of its blade cut one corner of the outlined square. The keratome incision also included as much of one border as possible without injury to the intraocular structures. A blade of special spring scissors with dull points was then passed beneath the cornea into the anterior chamber and one margin cut to the limbus. A narrow spatula replaced the scissors at the limbus,

and a cyclodialysis was performed to separate the root of the iris from the sclera (fig. 4). When this was accomplished, the remaining uncut borders were cut like the others with the special scissors. Great care was exercised to cut exactly along the outlined markings both in the cornea and in the sclera. When the square was removed it had a tendency to curl inward. It was placed on a piece of moist, sterile gauze and kept moist until the next step of the operation was completed.

Completion of Transplantation.—Two per cent fluorescein was instilled into the eye of the anesthetized rabbit and the excess washed off with saline solution. The markings became more visible, and the scissors could be used with greater accuracy. With the eye fixed at the limbus opposite to the site of the keratome incision, the anterior chamber was entered in the same manner as before. The fixation forceps was removed, and the operator used the previously placed central suture to steady the cornea while the special scissors completed the removal of the square, the edges being beveled to 20 degrees from the vertical.

During the entire time the anterior chamber is open the assistant operator must be constantly dropping a 3 per cent solution of sterile sodium citrate in saline solution into the operative field. This procedure was found to eliminate the necessity, due to fibrin formed by the aqueous humor, of great rapidity in this portion of the operation. When fibrin forms, great difficulty is encountered with matting of the sutures.

The central suture facilitates the handling of the corneal square and at the same time prevents injury to the lens. The corneoscleral implant was placed in the opening formed, the wide spatula being used, and the continuous corneal suture gently made taut. The operator can best make the suture taut by starting at its beginning and using two small forceps without teeth to pull it up while the assistant elevates the loop with a narrow spatula and allows it to come down gently to the graft. This procedure was continued from the beginning to the end of the suture, and the knot was surgically tied away from the graft on one side. The pressure of the suture was gently equalized at the four corners and the center with the narrow spatula and toothless forceps. The instillation of 3 per cent sodium citrate in saline solution was discontinued, and if an exact approximation of the graft had been achieved the anterior chamber was seen to fill quickly and no fibrin appeared in the conjunctival cul-de-sac.

Three per cent atropine sulfate was instilled, 1:2,500 metaphen ointment was placed in the conjunctival sac and the lids were sutured together with fine silk suture thread. A narrow gauze strip, enough to approximate the lids, was impregnated with 6 per cent colloidin in ether and placed gently over the eyelids as a dressing.

Postoperative Care.—The animal was carefully placed on his side in a cage, and he slept for several more hours. The dressing was not disturbed until the fourth or fifth day. It was then removed, the lid sutures were cut away and 1 per cent pontocaine was instilled into the eye to allow removal of the corneal suture. An assistant held the lids apart, and the suture was cut at the center crossing and removed. Three per cent atropine sulfate was instilled, 1:2,500 metaphen ointment placed in the sac and a similar gauze dressing applied to the lids. At the end of two more days the dressing could be entirely removed. Three per cent atropine sulfate was instilled according to the condition of the eye at subsequent examinations.

OBSERVATIONS ON CORNEOSCLERAL GRAFTS IN LIVING RABBITS

The observations to be recorded were made on a series of 16 corneoscleral grafts in the eyes of rabbits.

The rabbits were examined daily for several days after the dressing had been completely removed. Thereafter progress was noted at least three times a week until the final observation had been made, in the twentieth week. A complete record of each transplantation was thus accumulated.

At each examination the following points were noted: type of union of the graft, transparency of the graft, condition of the scleral implant,

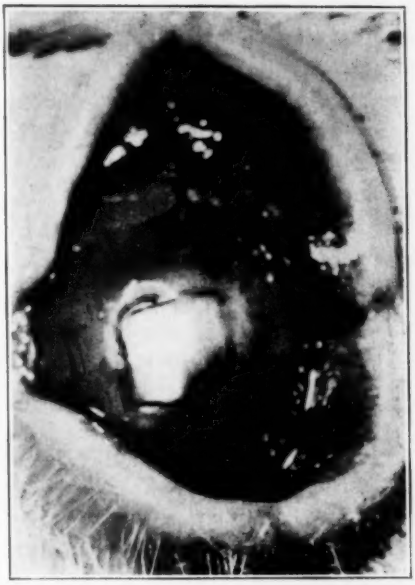

Fig. 5.—Corneoscleral graft, showing gaping of the superficial layers of the wound margins (× 3).

thickness of the graft, vascularization of the graft and the cornea of the host, condition of the cornea adjacent to the corneoscleral graft and the conjunctival reaction.

Union of the Graft.—Corneoscleral transplantation into the eye of the rabbit will successfully unite the graft with the cornea of the host. The union in this series appeared firm in the deeper layers when the sutures were removed on the fifth day. Slight gaping in the superficial layers could often be noted at this time. This was more marked in the scleral margin (fig. 5).

This deficiency in the scleral margin superficially was gradually filled in from the surrounding cornea of the host. In 7 animals, although the

union appeared firm at the fifth day, when the eye was examined the next day the anterior chamber was somewhat more shallow than it had been previously. This change indicated a slight loss of aqueous humor, due probably to too weak a union. However, the anterior chamber quickly regained its normal depth, and the graft became firmly united.

Transparency of the Graft.—The corneal portion of the graft remained transparent for the first week in all the animals. It was edematous and therefore assumed a bluish gray translucency, but the structures in the anterior chamber could be seen clearly through it. With the subsidence of the edema it began to show signs of nebulosity. By the second or third week it usually was markedly nebulous, and the iris could be seen only with difficulty through it. This progressive opacification was always associated with the rapid pannus formation in the cornea of the host, growing toward the graft. In 3 of the grafts, at about the sixth or seventh week a slight decrease in the nebulosity was apparent in the corneal portion. This change was preceded by a regression in the profuse vascularization of the cornea of the host, noted usually at the sixth week. In no animal was clearing of the nebulosity in the cornea at all marked or progressive, and it was noticed for only one or two weeks. In all the animals the cornea of the graft was almost opaque or completely opaque when the eye was removed for microscopic study at the twentieth week (fig. 6).

Scleral Portion of the Graft.—In the majority of the animals the fate of the implanted sclera was almost uniform. In all the grafts the surface of the scleral portion was rough and uneven for about the first ten days, after which the epithelium from the surrounding cornea of the host covered it and the surface became smoother. The graft showed a remarkable ingrowth of small capillaries beneath the epithelium over the scleral portion at the end of the first week in 1 case and at the end of the second week in another. This vascularity disappeared within two to four weeks.

The question of whether or not the scleral portion of the graft would be absorbed was particularly noteworthy. For the first three or four weeks no appreciable change in its size was observed. Then there was some slight absorption of the sclera, and it appeared definitely smaller than it had previously. The absorption was slow, and from the end of the eighth week no further reduction was noted (fig. 6).

There were 3 grafts in which unusual absorption of the sclera occurred. In 1, on the eleventh day apparent necrosis was noted in the scleral portion of the graft, and there was a subsequent increase in its absorption. By the fourth week the sclera had almost disappeared, leaving in its place an elevated opaque area. In this instance the unusual absorption was probably associated with the extreme vascularization of

the cornea of the host. In the second graft there was rich subepithelial vascularization over the sclera, and by the tenth week the sclera was almost completely absorbed. In the third graft the scleral portion began

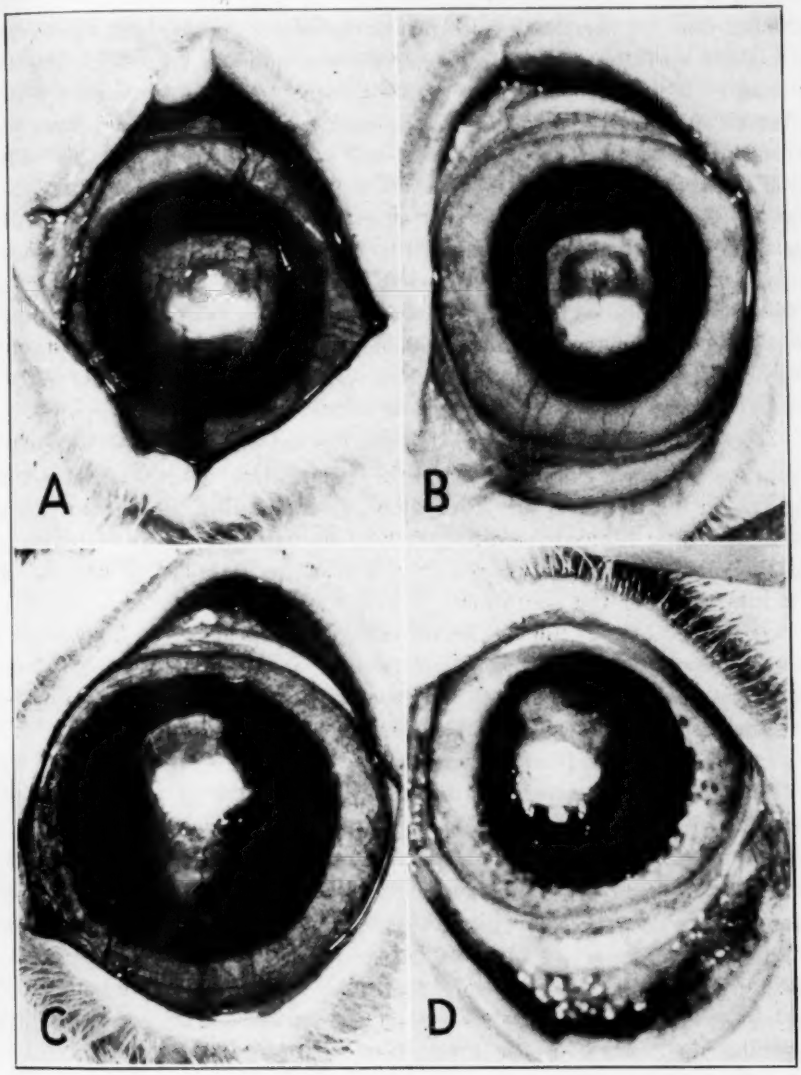

Fig. 6.—Corneoscleral grafts in place (× 3). *A*, nebulosity of the cornea in and around the transplant and pannus formation running toward the scleral portion. *B*, *C* and *D*, opacification of the cornea in the graft with interstitial vascularization of the cornea of the host.

to disappear at the end of the third week, so that little sclera could be observed with the corneal microscope by the tenth week. In all 3 eyes marked interstitial vascularization of the cornea of the host was present.

Thickness of the Graft.—On completion of the corneoscleral transplantation the surface of the cornea of the host and that of the graft were on the same level. This condition soon changed with the onset of edema in the graft, so that by the fifth day the graft appeared considerably thicker than the surrounding cornea of the host. As the edema subsided the slight elevation of the graft over the surrounding cornea diminished likewise. However, the thickness of the implant always remained slightly greater than that of the cornea of the host. This most probably was the result of the marked fibroblastic response within the graft. It was noted that the center of the transplant seemed to be the site of greatest thickness. This finding was characteristic of almost all the grafts, and the relation of the thickness of the graft to that of the cornea of the host was usually uniform. One striking exception was noted. In 1 animal, at the end of the second week the graft appeared almost two and a half times as thick in the central portion as the surrounding cornea of the host, and only a slight decrease in the thickness resulted eventually. Microscopic study of the sectioned eye revealed an excessive fibroblastic response.

Vascularization of the Graft and the Cornea of the Host.—Vascularization of the cornea of the host and the corneoscleral graft was a constant finding in this experiment. Fine blood vessels within the cornea of the host were first noticed from the sixth to the eighth day in the majority of the rabbits. They appeared in a few of the animals as late as the twelfth day after the operation.

It was noted that the first blood vessels to appear at the limbus were not necessarily opposite the scleral portion of the graft, as might have been expected. The vessels as a rule began to penetrate the cornea of the host at the upper limbus and from this point grew toward the graft. No rule was followed in placing the graft with respect to the position of the scleral portion. In some eyes this was nearer to the upper limbus, and in others it was nearer to the lower limbus.

At the end of two weeks the pannus had usually progressed 2 to 3 mm. and thus was growing rather rapidly. Examination with the slit lamp at this period showed that the vessels were derived from the conjunctival blood vessels. They lay between the superficial lamellas of the substantia propria of the cornea of the host. The vessels were bright red and branched arborescently. The pannus continued to grow rapidly, reaching the margin of the graft from three to four weeks after the operation.

During the first three to four weeks this rapid vascularization of the cornea of the host took place from the superior limbus over the upper one third of the corneal surface. However, at about the time when the vessels had reached the graft, new vessels appeared at the limbus in its remaining circumference. These capillaries in the same way penetrated

the corneal stroma of the host to reach the graft at the sixth week. Thus, at this period, the cornea was markedly vascularized over almost its entire extent and the vascularization had penetrated into the graft.

There was always a large number of small capillaries in the corneal stroma of the host immediately adjacent to the graft. Few vessels seemed to penetrate into the actual substance of the corneoscleral implant, but vessels could be seen with the slit lamp in the nebulous subepithelial and endothelial layers, i. e. superficially and deep into the actual corneoscleral graft. Here, too, the vessels were bright red and branched arborescently, forming an irregular anastomosing network. The vessels in the subepithelial and endothelial lamellas were derived from the anastomosing capillary network in the cornea adjacent to the graft.

Beginning at the sixth to the eighth week (the third week in 2 of the animals) a remarkable regression in the rich pannus formation occurred within the cornea of the host. The many fine vessels in the superficial lamellas of the substantia propia gradually disappeared, leaving in their wake a much smaller number of vessels of larger caliber. In many of the animals these larger vessels were prominent near the scleral portion of the graft (fig. 6 *A*, *B* and *C*). In a few, several equally large blood vessels were observed running toward the corneal portion of the graft (fig. 6 *A* and *C*). Thus the location of the larger vessels remaining after the intense pannus had subsided was not always constant. No remarkable changes in the interstitial vascularization of the graft or the cornea of the host were noted after the tenth week.

Cornea of the Host Adjacent to the Corneoscleral Graft.—The cornea of the host adjacent to the corneoscleral graft remained relatively transparent until the sixth week notwithstanding the intense pannus present. With the onset of regression of the fine interstitial keratitis at this time, the cornea of the host became slightly nebulous adjacent to the graft. From the sixth to the tenth week the nebulosity increased in intensity and extended 0.5 to 1.5 mm. into the cornea around the graft. Its extent varied somewhat (fig. 6 *A* and *D*). The cornea of the host external to the graft and the nebulous margins remained relatively transparent even though the interstitial vascularization did not completely disappear.

Within the corneal stroma adjacent to the corneoscleral graft a rich branching capillary network could be observed with the corneal microscope. This plexus of small vessels sent fine arborescent capillaries into the subepithelial and the endothelial layer of the graft.

Conjunctival Reaction.—The bulbar and the tarsal conjunctiva were very congested at the first dressing, on the fifth day. Marked ciliary injection was present. There was considerable hyperemia of the conjunctiva for two weeks, after which the eye gradually became white.

MICROSCOPIC STUDY OF THE CORNEOSCLERAL GRAFTS

A microscopic study was made of 16 transplants. The great majority of the sections were stained with hematoxylin and eosin, while a small number were stained either by a modified Cajal trichromic or the Van Giesen method.

The corneas of the sectioned eyes were systematically studied as to the following points: fibrin in the wound, epithelium, subepithelial fibroblasts, endothelial fibroblasts, sclera in the graft, cornea in the graft, vascular plexus around the graft, vascularization of the graft, nuclear content, spaces in the graft and perilimbal hyperemia.

Fibrin in the Wound.—There is a tendency in all corneoscleral grafts toward imperfect union of the transplant. The wound is immediately filled with fibrin, which is present in the aqueous humor. If an accurate approximation of the margins of the graft with the cornea of the host was obtained, a small amount of fibrin was observed in the intermarginal space (fig. 7). However, if the gap was considerable, more fibrin was seen (fig. 7 *B*).

This fibrous coagulum formed a scaffolding for the infiltration of fibroblasts at the end of the first week. These cells could be seen binding the lamellas together in the intermarginal space (fig. 7 *A*).

Epithelium.—Within forty-eight hours the epithelium of the host could be seen penetrating the wound margin. At this stage much of the epithelium covering the graft was lost. This soon was replaced from the host. However, such regeneration of epithelium is complicated by a marked fibroblastic response beneath the basal cells of the epithelium. Hence, normal epithelial cells are rarely found in corneoscleral grafts. The epithelium was frequently thin, and the normal six epithelial rows of the rabbit were reduced to two or three in places. In the same section with thin epithelium, unusually thick and uneven epithelium was often seen. Here, ten to twelve rows might be observed. This marked unevenness in the epithelium was a characteristic finding (fig. 8).

Some of the sections exhibited a remarkable bullous formation within the epithelial layer, with one or several small cysts, or bullae.

Where the epithelium was thinned the normal cylindric basal cells were replaced by low cuboid cells with deeply staining nuclei. In this area the wing cells were often completely lacking and there might be found only two or three surface rows composed of flattened cells with flat nuclei. Where the epithelium was thickened as many as twelve rows were counted. Here the basal cells were columnar, each with an oval nucleus, while six to eight rows of polyhedral wing cells containing oval or round nuclei were present more superficially.

Subepithelial Fibroblasts.—Almost always, after the first week there was a layer of cells deep to the epithelium and in front of the implanted

Fig. 7.—Corneoscleral grafts (× 150), showing (*A*) fibrin in the intermarginal space and (*B*) a gaping wound containing a fibrous coagulum.

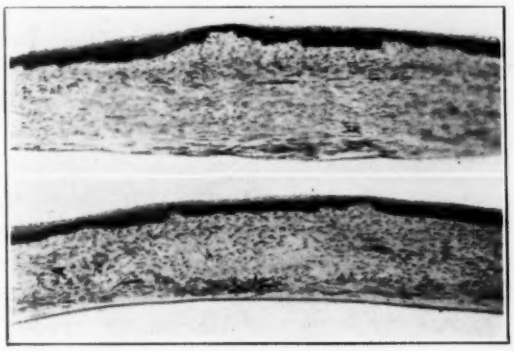

Fig. 8.—Corneoscleral grafts, showing irregularity of the epithelium (× 150).

cornea and sclera. This layer was continuous with, and apparently derived from, approximately the anterior half of the adjoining cornea. It encased the graft on its anterior aspect.

The fibers had the appearance of fibroblasts. They were closely packed in lamellas with many flat, thin, well staining nuclei. The cells were long, pointed and straight, and they ran more or less parallel to one another.

The thickness of this layer was an important factor in determining the thickness of the graft. It might consist of relatively few lamellas, or it might be thicker than the actual graft itself (fig. 9*A*).

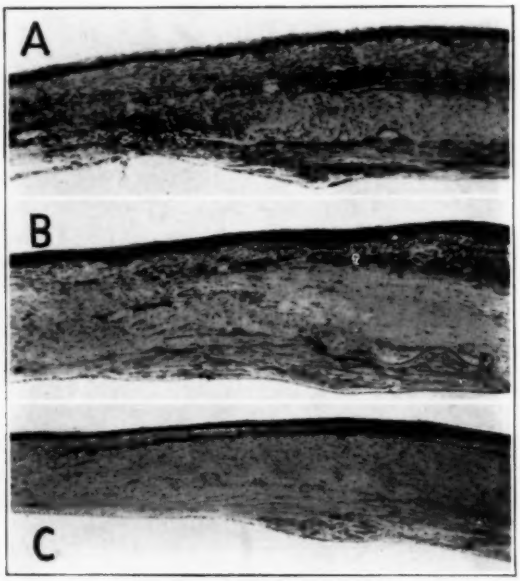

Fig. 9.—Corneoscleral grafts, showing subepithelial and endothelial infiltration of fibroblasts (× 150).

The subepithelial fibroblastic layer was usually of constant thickness from the center to the ends, where it quickly terminated as a thin layer. No tendency for the fibroblasts to invade the graft as the layer passed over it was shown.

Fine capillary blood vessels could be seen in this subepithelial layer of fibroblasts. These vessels had their origin in a plexus of vessels which lay in the stroma around the graft. Branches from this plexus ran anteriorly and posteriorly to the graft and could be seen ramifying between the fibroblasts which lay adjacent to the implanted cornea and sclera. A perivascular leukocytic infiltration was frequently seen.

Endothelial Fibroblasts.—As mentioned before, along with the infiltration of fibroblasts anterior to the implanted cornea and sclera, there was a similar infiltration posteriorly after the first week. This layer of endothelial fibroblasts was limited superficially by Descemet's membrane and deep to it by the endothelium. The fibroblasts were derived from the endothelial cells and the deepest fibers of the adjoining corneal stroma. They encased the graft on its posterior aspect. Their appearance was similar to that of the fibroblasts anterior to the graft; i. e., they were elongated, flat, straight cells parallel to one another and containing thin, well staining nuclei.

The thickness of the layer of endothelial fibroblasts was fairly constant from the center to the ends, where it tapered somewhat. However, the number of lamellas appeared more uniform than in the layer of subepithelial fibroblasts, the thickness varying from one half of to almost the same as that of the implanted cornea and sclera (fig. 9 *B* and *C*). Like the subepithelial fibroblasts, the endothelial fibroblasts showed no tendency to invade the fibers of the graft as they passed behind them.

Capillaries were found between the endothelial fibroblasts also and were derived from the plexus of vessels which lay in the stroma around the graft.

This formation of subepithelial and endothelial fibroblasts after the first week probably was an important causative factor in the onset of nebulosity within the graft at that time. With the increase in the number of fibroblasts, the graft finally became more opaque. At the same time its vascularization assisted in the production of nebulosity and opacification.

Sclera in the Graft.—In sections from normal eyes no line can usually be distinguished separating the cornea from the sclera, since the fibers of the one are continuous with those of the other. A similar observation was frequently made in the microscopic study of the corneoscleral grafts in this series. In many sections it was not possible to distinguish the implanted cornea and sclera with any degree of certainty. However, the presence of Descemet's membrane posterior to the graft indicated corneal tissue, while the tissue was considered to be sclera when Descemet's membrane was not present posteriorly.

When the scleral portion of the implant could be satisfactorily identified, it was observed that the normal dense feltwork of connective tissue bundles was little altered. The amount of sclera to be seen microscopically did not seem to be greatly diminished from that which had been transplanted. Absorption of the sclera was minimal except when complications were present. Three of the eyes showed remarkable

absorption of the sclera, and in these either necrosis or profuse vascularization had taken place.

In a few of the sections the sclera could be easily identified by the presence of whorls of connective tissue cells and elastic fibers. These sections probably contained more elastic fibers than the others, and the nuclei were thus irregular. The nuclear content of the implanted sclera did not seem to be increased. These sections showed little evidence of absorption of the sclera (fig. 10).

Many fine capillaries were characteristically observed superficial to the implanted sclera. They were present between the fibroblasts in the deeper portion of the layer. No tendency for the capillaries to invade the implanted sclera was noted, and the sclera remained avascular

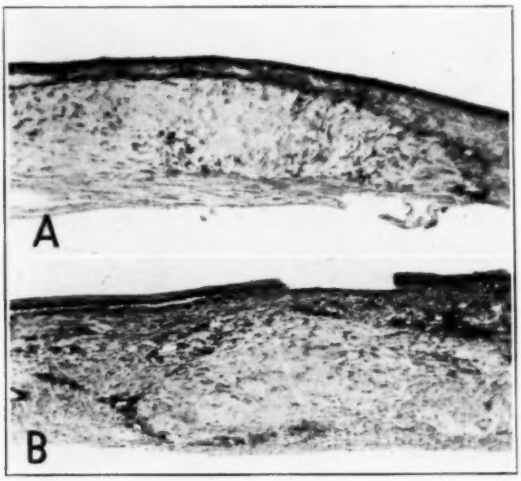

Fig. 10.—The scleral portion of corneoscleral grafts (× 150).

(fig. 10 *B*). Few capillaries were seen deep to the graft within the endothelial fibroblasts.

Cornea in the Graft.—When the implanted cornea was capable of being differentiated from the sclera according to the methods mentioned previously, fairly uniform observations were made.

The grafted cornea in the beginning was separated from the cornea of the host by an intermarginal coagulum of fibrin. At about the fifth day fibroblasts were seen in this coagulum, and toward the end of the third week fine capillaries had penetrated its substance.

The marginal limits of the corneoscleral graft were rounded off, being largely encircled by the new tissue of fibroblasts anteriorly and

posteriorly. At each end the stroma might taper to a point. This tended to exclude it from direct continuity with the tissue fibers of the recipient eye.

The normal parallel lamellas of the substantia propria were usually observed. However, the posterior half of the stroma of the corneal portion of the graft was somewhat amorphous and contained few nuclei in a given area. The nuclei were less in number than in the stroma of the adjacent cornea of the host and much less in number than among the subepithelial and the endothelial fibroblasts. They were large and flattened and stained less deeply than those in the adjoining layers of fibroblasts (fig. 11 *A*).

Capillaries were seen superficially to the corneal portion of the graft within the deeper lamellas of fibroblasts, while fewer capillaries were

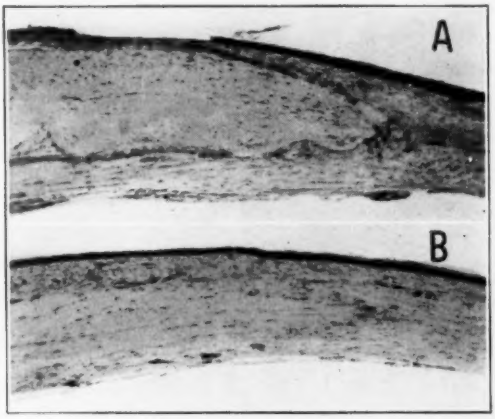

Fig. 11.—The corneal portion of corneoscleral grafts (× 150).

present within the layer of endothelial fibroblasts. As in the scleral portion of the graft, little tendency was noticed for the vessels to invade the corneal implant (fig. 11 *B*).

Vascular Plexus Around the Graft.—A constant observation in all the sections was the presence of blood vessels within the stroma of the host immediately adjacent to the transplant. The vessels were small branching capillaries, and they formed a rich plexus which sent many small branches into the subepithelial and the endothelial layer of fibroblasts. A marked perivascular infiltration of lymphocytes was present around the graft (fig. 12 *A*).

The blood vessels were mostly derived from the conjunctival vessels. These vessels, along with some of the deeper ciliary vessels, sent an interstitial network through the stroma of the host toward the graft.

The vessels could be observed first from the sixth to the twelfth day. Most of them lay in the anterior layers of the stroma of the host. At the fourth week they reached the junction of the cornea of the host and the graft, where an anastomosing plexus was formed around the graft (fig. 12 *A*).

Vascularization of the Graft.—In all the eyes in which the transplantation was without complications, the vascularization of the graft was confined mostly to the subepithelial and the endothelial layer of fibroblasts. More vessels were observed in the subepithelial layer than in the endothelial layer. The capillaries were present about the fourth week, and they were seen lying close to the implanted cornea and sclera but within the layers of the fibroblasts. Around the vessels there was an

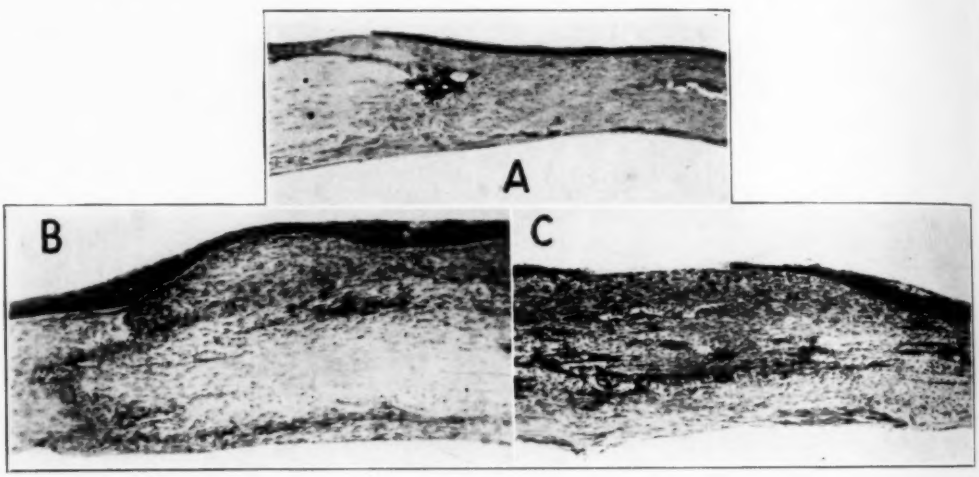

Fig. 12.—Corneoscleral grafts (× 150), showing (*A*) a surrounding vascular plexus, (*B*) marked interstitial vascularization of the graft and (*C*) wrinkling of Descemet's membrane.

infiltration of lymphocytes. This leukocytic cupping of the vessel was lance shaped because of compression by the fibroblasts.

The corneoscleral graft itself remained comparatively free from invasion by blood vessels in the majority of instances. However, the blood vessels were abundant in a few of the sections. Infection of the graft was a predisposing factor. The vessels were large, and the perivascular cupping was prominent (fig. 12 *B*).

Descemet's Membrane.—The normal curve of Descemet's membrane was replaced in the corneoscleral grafts by a pronounced wrinkling over the entire extent of the transplant. The degree of folding was commonly marked (fig. 12 *C*). No new Descemet membrane was to be

found in the sections. The cut ends of this membrane were separated at the corneal margin of the grafts. The ends had a tendency to curl outward. Considerable fibroblastic tissue, with an occasional small blood vessel, was present between them (fig. 12 *C*).

Thickness of the Graft.—Microscopic sections of the corneoscleral grafts within the first week showed the edematous nature of the transplant. There was an increase in the thickness of the graft as compared with the cornea of the surrounding host. A study of the sections after the infiltration of the graft by fibroblasts revealed the varying degree of thickness that may eventually result after corneoscleral transplantation. In all the grafts an increase in thickness was to be seen. The thickness was in direct proportion to the amount of fibroblastic tissue present superficial and deep to the graft (fig. 9 *B*).

Nuclear Content of the Graft.—Changes in the nuclear content were uniformly observed.

At the end of forty-eight hours the nuclei within the transplant were in a state of fragmentation. They appeared less in number, and they did not stain deeply. If the union of the graft to the cornea of the recipient eye was poor and iris adhesions were present, a great increase in the number of nuclei was observed. By the twelfth day the graft showed an enormous number of deeply-staining flattened nuclei running more or less parallel to one another. Irregular spaces between the fibers were frequently seen when the nuclear content of the graft was increased.

In the eyes in which transplantation was with complications, at the second or third week subepithelial and endothelial infiltration of fibroblasts was plainly seen. In the sections from these eyes there was a generalized increase in the nuclear content of the transplant within these layers. The nuclei stained deeply and were flattened in more or less parallel rows (fig. 9 *A*). This remarkable increase in nucleation was associated with vascularization in the fibroblastic layers. It also was an important factor in the increase of the thickness of the graft.

The nuclei were more numerous in the subepithelial and the endothelial fibroblastic layer than in the actual graft. The posterior half of the stroma of the implanted cornea was amorphous and contained fewer nuclei in a given area than the superficial half of the stroma in a similar area. Also, the number of nuclei was less than in the stroma of the adjacent cornea of the host. The nuclei were somewhat larger and more flattened and stained less deeply than those in the adjoining layers of fibroblasts. There was some decrease in the number of nuclei within the grafted sclera. Here the nuclei were irregular and often were arranged in whorls (fig. 10 *B*). A single layer of well staining endothelial cells lined the corneoscleral graft posteriorly.

Spaces in the Graft.—Irregular spaces, some of which were spindle shaped, were frequently observed between the fibers of the corneoscleral grafts. These spaces were usually greatest when the nuclear content of the transplant was increased. They were most commonly present within the subepithelial layer of fibroblasts in its deeper portion (fig. 13). However, they were also seen within the superficial portion. The spaces were less commonly encountered within the endothelial layer of fibroblasts.

Perilimbal Hyperemia.—The blood vessels in the region of the limbus of the recipient eye were markedly congested until about the end of the second week. Both the conjunctival vessels and the deeper ciliary vessels were dilated and contained many erythrocytes and polymorphonuclear leukocytes. There was an infiltration of leukocytes into the conjunctival tissue which produced a slight chemosis of the bulbar conjunctiva. This vascular congestion disappeared in about two weeks.

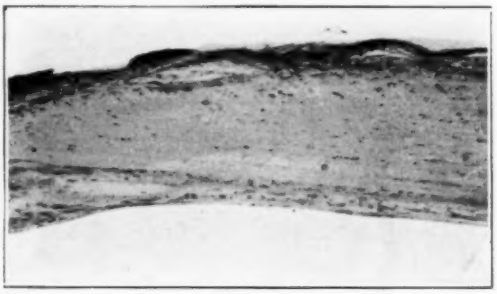

Fig. 13.—Irregular spaces in a corneoscleral graft (× 150). These are observed in the layers of subepithelial and endothelial fibroblasts.

ANALYSIS OF COMPLICATIONS ENCOUNTERED DURING THE EXPERIMENT

The complications which we encountered in corneoscleral transplantation will be briefly outlined. The pathogenesis of the complications has been noted in detail by Castroviejo.

Defective Coaptation of the Edges.—The most common complication was the imperfect coaptation of the edges. The transplanted square was cut either too large or too small, or the recipient corneal square itself was too large or too small. As a result the margins were not well apposed and fibrin formed between the lips of the wound (fig. 7 *B*). In many cases anterior synechias were present. These resulted always in a proliferation of fibroblasts behind the implant and vascularization of the stroma of the cornea of the host and the graft and often in an increase in the nuclear content of the graft (fig. 14 *A*).

Infection.—The second most common complication encountered was infection. When this took place, either fulminating panophthalmitis

with loss of the eye or vascularization with complete opacification of the graft was the outcome. Bacteriologic examination of the pus obtained showed the presence of Staphylococcus albus (hemolytic), Bacterium faecalis alcaligenes and Corynebacterium xerosis. Microscopic study of the eyes at the end of the fifth week revealed a great infiltration of the anterior layers of the graft with polymorphonuclear leukocytes and plasma cells (fig. 14 *B*). Some sections showed the formation of a corneal ulcer with the infection limited to the anterior half of the transplant.

Fig. 14.—*A*, section of a corneoscleral transplant in an eye in which anterior synechias developed (× 150). *B*, section of a corneoscleral graft in an eye in which an abscess of the cornea developed (× 150).

Improper Insertion of the Suture.—Not so commonly encountered was the improper insertion of the suture. The suture was at times placed either too close or too far from the margin of the graft. On other occasions it was inserted too deeply, with consequent loss of the aqueous humor, or it was inserted too shallowly and thus loosened itself. Once the knot became united before the usual time for removal of the suture. In all these instances the transplant was either defective or failed to take at all.

Rupture of the Anterior Capsule of the Lens.—Several of the transplant operations were complicated by a poor keratome incision, and the point of the instrument opened the anterior capsule of the lens. If this fact was noted at the operation, an extracapsular extraction of the lens was performed. Otherwise it was noticed at the first dressing because of the presence of a traumatic cataract and sloughing of the transplant.

Loss of the Dressing.—Infrequently, the rabbit was irritated by the dressing which had been applied to close the lids, and by the first examination after the operation he had rubbed off several of the dressings. In such instances the transplant was frequently dislodged.

Formation of Fibrin.—The transplantation must be performed with considerable rapidity if the operator is to avoid the matting of the sutures by fibrin. Once fibrin has formed the sutures become entangled by it, and this adds to the difficulty of the operation. However, if an anticoagulant, such as 3 per cent sodium citrate solution, is dropped onto the operative field, rapidity is not necessary.

It is apparent that corneal transplantation requires considerable skill. However, the technical difficulties are not insurmountable, and this description of the complications may be of assistance to other investigators wishing to perform the operation on animals.

SUMMARY

Corneoscleral transplantation was performed on 16 rabbits during this experiment.

The method is described in detail. The corneoscleral transplant was obtained from the limbal region, so that a 4 mm. square contained 3 mm. of cornea and 1 mm. of sclera.

There was a tendency in all instances toward imperfect union of the graft. A slight gaping was noted along the scleral wound margin in its superficial layers.

The epithelium over the corneoscleral graft was replaced by an uneven growth of epithelium from the recipient cornea.

After the first week a marked proliferation of subepithelial and endothelial fibroblasts was noted. The layers of these cells encased the implant. The subepithelial fibroblasts were derived largely from the anterior portion of the stroma of the recipient cornea, while the endothelial fibroblasts were formed from the endothelium and the deeper corneal fibers.

The corneal portion of the graft remained transparent for the first week, after which it became nebulous and later opaque. The onset of nebulosity and opacification was associated with the proliferation of fibroblasts and blood vessels in the graft.

The scleral portion of the graft began to be absorbed slightly about the third or fourth week. After the eighth week no further absorption was noted. In 3 instances unusual absorption occurred. There was marked interstitial vascularization of the recipient cornea in these instances.

The corneoscleral grafts were thicker than the cornea of the host. Their thickness was due to proliferation of the subepithelial and the endothelial layer of fibroblasts and consequent nuclear increase within the graft.

Blood vessels were noted growing in the cornea of the host from the upper limbus from the sixth to the twelfth day. The vessels finally involved the entire cornea and invaded the layers of fibroblasts encasing the graft about the third or fourth week. A rich arborescent plexus surrounded the margins of the graft, but few vessels invaded the actual implanted cornea and sclera.

There was pronounced wrinkling of the Descemet membrane in the graft. However, no evidence of the formation of a new Descemet membrane was observed.

The nuclear content of the graft was greatly increased in the layers of fibroblasts, but the nuclei in the implanted cornea and sclera were diminished in number and stained poorly.

Irregular, spindle-shaped spaces were frequently observed within the layers of fibroblasts.

An analysis of the complications encountered during the experiment is outlined. These included defective coaptation of the edges, infection, the results of improper insertion of the suture, rupture of the anterior capsule of the lens and matting of the sutures with fibrin.

CONCLUSION

A study of corneoscleral transplantation in rabbits led to the conclusion that such grafts can unite with the host but that the union tends to be imperfect. The transplants invariably become opaque and vascularized.

Corneoscleral transplants have many of the characteristics of heterogenous grafts. The epithelium over the corneoscleral graft is lost, and it is replaced by an uneven growth of epithelium from the recipient cornea. The epithelium is supported by a subepithelial layer of fibroblasts derived largely from the stroma of the recipient cornea. Behind the graft a layer of fibers is formed from the endothelium and the deep corneal fibers of the host. A rich vascular plexus surrounds the graft and sends arborescent fine capillaries into the layers of fibroblasts superficial and deep to the graft. The original stroma of the graft can be

distinguished as a mass of poorly staining fibers with few nuclei and practically no blood vessels. It is encased largely by the subepithelial and endothelial fibroblasts. The scleral portion of the graft is diminished little in size. Descemet's membrane remains, but it is frequently wrinkled.

Thus, the conception is warranted that scleral tissue included in corneal grafts transplanted into the eyes of rabbits is a tissue tolerated but largely ostracized by the recipient eye. The inclusion of sclera is therefore undesirable, and it should be avoided in corneal transplantation in man.

OPERATION FOR REMOVAL OF PTERYGIUM

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The fact that there are so many operative methods for the removal of pterygiums shows that until now none of them has given entirely satisfying results to all surgeons. Therefore a method is described which I developed in association with Dr. C. Iklé when in charge of an ophthalmic department in Switzerland. There, as in private practice, the results were uniformly satisfactory, and up to this writing there has been no recurrence. The operation does not advance anything fundamentally new, being combined with other plastic procedures. However, it is the combination and the addition of some important details that gives greatly improved results.

A pterygium can give rise to two types of impaired vision: In advanced stages it causes a partial or complete opacity of the pupillary region of the cornea, and in the early stages it often causes astigmatism by reason of flattening of the corneal curvature, which may be associated with a pigmented line giving the impression of breaks in Bowman's membrane.[1] It also tends to recur.

According to Ziegler[2] a pterygium has to be removed (1) when it is progressive, (2) when it interferes with vision, (3) when it limits ocular mobility, (4) when a major operation on the globe is planned and (5) when it is cosmetically disfiguring.

To these conditions should be added: (6) as soon as astigmatism occurs.

According to my experience a pterygium tends to recur (1) when, particularly in the limbal region, it has not been removed sufficiently inferiorly and superiorly and as deeply as the underlying sclera; (2) when there is any scarring, and (3) when large conjunctival vessels and strands of fibrous tissue extend in a horizontal direction toward the limbus in the region where it had been located.

The operation, therefore, should be so executed as to:

1. Result in a transparent cornea. To this end it is necessary that the lesion be completely removed from its head as far as the limbus, no trace whatever of it remaining on the corneal segment.

1. Stocker, F.: Eine pigmentierte Hornhautlinie beim Pterygium. (Beitrag zur Entstehung von Brüchen in der Bowmanschen Membran, Klin. Monatsbl. f. Augenh. **102**:384, 1939.

2. Ziegler, S. L.: The Subconjunctival Excision of Pterygium, Internat. Cong. Ophth. **1**:206, 1922.

2. Bring about as complete a dissection of the conjunctival part of the pterygium as possible, the operator taking particular care to remove a sufficient amount on both sides and to go as deep as the sclera, since a new membrane can arise from any residue.

3. Eliminate the placing of sutures, which are necessary in most of the usual operative methods, in the area previously occupied by the pterygium, as any scarring in this region can give rise to a recurrence.

4. Change the course of the large conjunctival vessels or strands of tissue from a horizontal direction. They should be made to go in a direction opposite to that of the pterygium.

A review of the literature reveals that Campodonico [3] was the first to point out these factors and to develop his operation accordingly. His method, however, was based on a complete excision of the lesion, which in cases of an extensive growth is not feasible. Spaeth's [4] method of the "rotated island graft" is also aimed at preventing a recurrence, but it has the disadvantage that the lesion remains at its original site, although in a rotated or cross position, and its proper tissue remains in contact with the limbus. Other plastic methods, described by Desmarres,[5] Czermak [6] and Knapp,[7] either leave part of the area formerly occupied by the pterygium uncovered or require the insertion of sutures there.

The procedure recommended here is as follows:

1. Local anesthesia is induced by instillation of 1 per cent solution of pontocaine hydrochloride and subconjunctival injection of about 0.5 cc. of 2 per cent solution of procaine hydrochloride with epinephrine.

2. The pterygium is grasped with a forceps near its head, and with a cataract knife, beginning at the end nearest the pupillary area, the operator dissects it from the underlying corneal parenchyma as far as the limbus with cuts directed obliquely (*A* in the accompanying illustration). This procedure is preferable to inserting the knife under the pterygium at the limbus and cutting toward the center of the cornea. It has been found by several other surgeons also that reversing the

3. Campodonico, E.: A New Procedure in the Excision Method for the Cure of Pterygium, Internat. Cong. Ophth. **1**:201, 1922.

4. Spaeth, E. B.: Rotated Island Graft Operation for Pterygium, Am. J. Ophth. **9**:649, 1926.

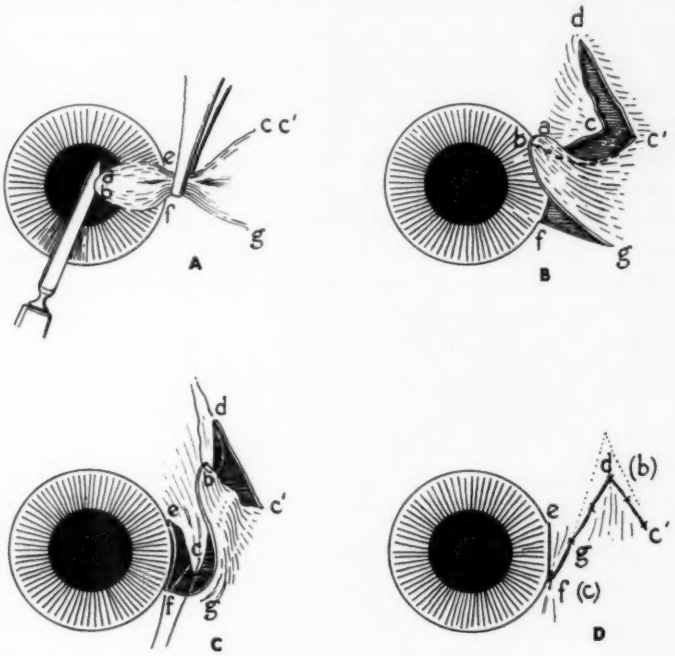
5. Desmarres d'Evreux, L. A.: Traité théorique et pratique des maladies des yeux, Paris, Germer-Baillière, 1855, vol. 2.

6. Czermak, W.: Die augenärztlichen Operationen, Vienna, C. Geralds Sohn, 1890, vol. 2.

7. Knapp, H.: Ueber einige neue namentlich plastische Conjunctivaloperationen, Arch. f. Ophth. **14**:267, 1868.

direction, i. e. beginning at the pupillary area, provides better control as to the depth of the dissection necessary to remove the lesion completely. Should any grayish areas remain, they must be removed with the knife or a curet.

3. From the limbus outwardly, along the upper (*A, e-c*) and the lower (*A, f-g*) margin of the lesion, the conjunctiva is incised with straight scissors, the upper incision being at least as long as the breadth of the pterygium at the limbus (*A, e-f*). The lower incision should be about half as long as the upper one.



The operative procedure (drawings by Mr. E. G. Bethke, of the Ophthalmological Institute of the Presbyterian Hospital).

4. Beginning at the limbus, the operator dissects from the underlying sclera backward as far as possible, although never as far as the semilunar fold.

5. The conjunctiva is loosened over a wide area along the upper incision. It is loosened along the lower incision to a much lesser extent and never as far as the limbus. This is important to the success of the following movement.

6. In the case of a pterygium located nasally, an incision upward and outward at an angle of approximately 45 degrees is made from the upper end of the conjunctival incision (*B, c-d*) forming a flap of

normal conjunctiva. A suture is placed in its apex (*C, c*) and fastened at the limbus (*C, f*), where the lower conjunctival incision started. The attachment here should be not only to the conjunctiva but to the episclera, as this prevents any shifting of the flap upward and eliminates sutures in the area formerly occupied by the pterygium.

7. The head of the pterygium is then excised obliquely with scissors (*B, b-c'*). In this way a flap with smooth edges is obtained. Furthermore, the degenerated tissue of the head if merely transplanted occasionally would become a source of irritation until absorbed.

8. A suture is placed in the apex (*C, b*) of the flap composed of the remains of the pterygium and fastened in the conjunctiva (*C, d*). A straight edge (*D, f-g-d*) is formed, which is connected with the edge *f(c)-d* by two or three sutures. The edges *c'-b* and *c'-d* are connected in the same manner.

It appears at first glance that this method of grafting would cause undue stretching of the flap. Experience has shown, however, that it does not, because, owing to the wide loosening of the conjunctiva in the region of the upper end of the conjunctival incision (*d* in *B, C* and *D*), it slips downward easily and, furthermore, the conjunctiva in itself has great adaptability.

As suture material, silk is preferable. It can be removed in from five to seven days if it does not free itself before then.

SUMMARY OF ADVANTAGES

1. No healthy tissue is removed.

2. No uncovered defect remains in the scleroconjunctival area.

3. The fixation of the grafted flap in the episclera at the lower edge, where the pterygium had been in contact with the limbus, eliminates the necessity of placing sutures in the region where the pterygium had been located.

4. The course of the pterygium, with its fibers and vessels, is directed vertically, and it is separated from the limbus by a flap of normal conjunctiva.

5. The blood vessels in the flap of sound conjunctiva covering the place formerly occupied by the pterygium have a course tangential instead of radial to the limbus.

ABSCESS-FORMING FOLLICULAR CONJUNCTIVITIS

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GRAND JUNCTION, COLO.

Diseases of the conjunctiva, with progressing knowledge of pathology, have received a standardized classification. Ophthalmologists are endeavoring to adapt clinical pictures more or less to this classification.[1]

The name follicular conjunctivitis signifies a large and important group of conjunctival diseases in which changes in the lymph follicles are in the foreground. Included under this name are heterogeneous conditions—acute and chronic diseases, well established entities and vague clinical pictures.

A diseased condition is reported here which differs from the other members of the group clinically and pathologically.

First some brief details about the lymph follicles of the conjunctiva will be mentioned. The lymphoid tissue develops in the conjunctiva in the first months of life in the form of an adenoid layer, mostly in the fornix and less in other parts. Normally it does not contain true lymph follicles. After irritation of different kinds the lymphocytes of the adenoid layer, instead of remaining evenly distributed under the epithelium, aggregate into follicles. This is the case, for example, in follicular conjunctivitis. The follicles apparently represent a tissue reaction to infective irritations.

The individual follicle (fig. 1) shows a light inner zone (*I*) in which large lymphocytes with feebly staining nuclei are arranged, with a dark ring of deeply stained small lymphocytes around them (*O*). In addition to these two types of cells, a third, large cell occurs in the interior; this has extraordinary phagocytic qualities and is probably histiocytic in nature.

These are the cells which build the follicles. It is important that polymorphonuclear leukocytes do not occur in follicles except sporadically and incidentally. Also, bacteria are entirely lacking in their interior.

The following cases represent findings different from these, the ones usually described. Case 1 has previously been reported,[2] but the nature of the pathologic process could only be hinted at.

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1. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1938, vol. 2.

2. Rigg, J. P., and Waldapfel, R.: Acute Abscess of the Lymph Follicles of the Conjunctiva, Arch. Ophth. **22**:882 (Nov.) 1939.

REPORT OF CASES

CASE 1.—A 35 year old woman had an inflammation of the left eye for three days, and the lids stuck together in the morning. She did not feel well generally, and the eye was painful and felt scratched. The temperature was 99.4 F. The right eye was normal. The nasal portion of the conjunctiva of the left eye was inflamed, and a mucopurulent discharge was present. Slight chemosis of the lower lid in the lower fornix and swollen follicles could be seen. About in the middle of the inflamed area of the bulbar conjunctiva, midway between the limbus and the caruncle, there was a small elevation with a yellowish center and a deeply inflamed halo.

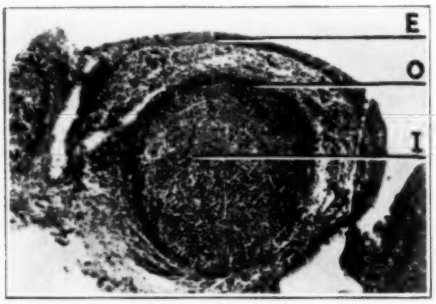

Fig. 1.—Lymph follicle of the conjunctiva. *E*, epithelium; *O*, outer zone, and *I*, inner, light zone. From Taborisky, J.: Zur Histologie des frischen Trachoms und der Follicularis, Arch. f. Ophth. **131**:174, 1933.)

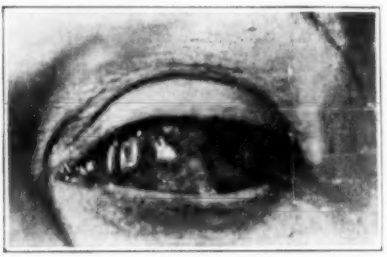

Fig. 2 (case 1).—The involved eye (black and white photograph with a green filter).

The elevation did not show any ulceration, but pus seemed to shine through at its tip. The diseased area was freely movable and confined to the conjunctival layer.

Figure 2 shows the diseased eye as well as it can be represented in a black and white photograph. The swelling and the deep vascularization of the bulbar conjunctiva are apparent. About in the middle of the inflamed area the elevation can be seen, with its yellowish center and the red halo around it.

Excision of the yellow area, which showed a small amount of pus, resulted in healing and a practically normal eye within three days. No microscopic examination was made.

CASE 2.—A 28 year old man had had a herpes of the forehead two months before. Four days before the right eye started to get red. The entire right side of the head hurt badly, and the patient felt sick generally.

Clinical Picture.—The left eye was normal. In the right eye (fig. 3 *A*) the bulbar conjunctiva temporally was swollen, edematous and hyperemic. Between the limbus and the external canthus—more toward the limbus—a circumscribed swelling about ⅕ inch (0.5 cm.) in diameter, with a slight inflammatory halo, was to be seen. On the tip of the swelling the color was more yellowish. The epithelium over the whole affected area was intact. The entire diseased area was confined to the conjunctiva and could be moved with it. Some swollen follicles could be seen in the upper and in the lower fornix. There was a mucopurulent discharge, and photophobia was present. Streptococci and staphylococci were the chief bacteria observed. There were no inclusion bodies.

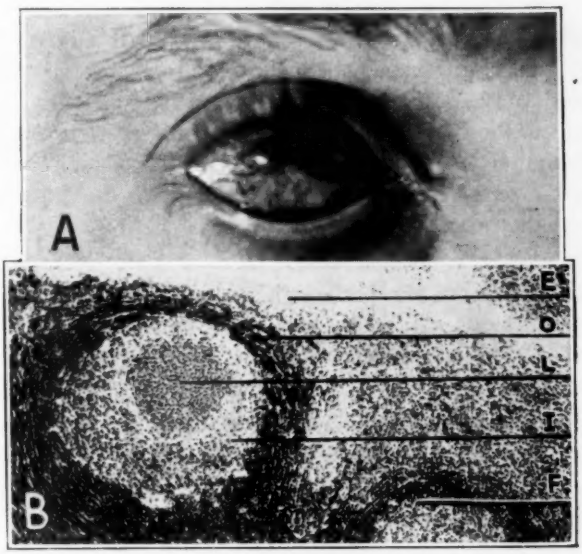

Fig. 3 (case 2).—*A*, the involved eye (kodachrome photograph, black and white print). *B*, microscopic section. *E*, epithelium; *O*, outer, dark zone of the follicle; *I*, inner, light zone of the follicle; *L*, miliary abscess within the light zone of the follicle, and *F*, part of another lymph follicle.

Excision.—Excision of the yellowish area, yielding a small amount of crumbly grayish matter, and administration of sulfanilamide internally and locally were followed by recovery within three days. One week later the site was normal and did not show any signs of the previous disease.

Microscopic Examination.—In the excised piece of conjunctiva (fig. 3 *B*), under the intact epithelium (*E*) an adenoid layer could be seen massed with lymphocytes and large subepithelial follicles, of which figure 3 *B* shows a complete one (*O*, *I*) and part of another (*F*). Both are distinctly differentiated into a dark external zone (*O*), consisting of deeply stained lymphocytes, and a lighter inner zone (*I*)—the so-called germ center—, containing the usual cells with feebly stained nuclei

and the large phagocytic cells. But, in addition to cells of the three types characteristic of follicles, polymorphonuclear leukocytes can be seen in the light inner zone; such cells are uncommon in this area. They are arranged in a fairly sharply limited circular aggregation (*L*) a little outside the center of the light area of the follicle, and thorough bacteriologic search of the section revealed streptococci within this leukocytic aggregation.

The presence of leukocytes or streptococci is abnormal in a follicle, and there is no doubt that this focus of leukocytes and cocci is to be regarded as a miliary abscess inside the follicle. Two such foci could be found in the sections of the excised piece. They explain the clinical appearance of the yellowish tip of the swelling under an intact epithelium.

COMMENT

The acute inflammatory disease of the conjunctiva in each case does not fit into any of the established classifications. In association with malaise, fever and a fairly strong local reaction, consisting of chemosis, photophobia and the presence of a mucopurulent secretion, a conjunctivitis of the follicular type developed, the main process being on the bulbar conjunctiva between the limbus and the internal or the external canthus. In both cases the process remained unilateral.

While in the first case, in which there was no microscopic examination, the character of the pathologic change could only be suggested, the microscopic examination in the second case established the nature of the process. It was an inflammation of the lymphoid tissue with formation of miliary abscesses in the lymph follicles.

This process is in analogy with infections of the lymphoid tissue in the pharynx. In acute tonsillitis and in acute inflammation of the adenoid tissue of the epipharynx, similar abscesses are to be found in the lymph follicles.[3] They appear at the climax of the disease in the light inner zones of the follicles centrally or excentrically situated.

The picture in these cases differed from the types of follicular conjunctivitis thus far described, and it would seem appropriate to differentiate the process as abscess-forming follicular conjunctivitis.

In view of the findings reported and the success in the treatment of similar infections of the pharynx, administration of sulfanilamide ought to be the method of choice.

The question of why conjunctivitis sometimes occurs in this form allows, in an era of allergic diseases and focal infections, numerous hypotheses. Streptococci are not normal inhabitants of the conjunctiva. They cause diseases of the eye in cases of general infection or—usually

3. Grossmann, B., and Waldapfel, R.: Lacunar Tonsillitis: Histopathological Study on a Clinical Basis, Acta oto-laryng. **10**:1, 1926.

—in cases of focal infection in an allergic person. It may be that infective streptococcic foci in remote parts of the body are responsible for the type of infection here reported.

SUMMARY

Two cases of infection of the conjunctiva are reported in which minute aggregations of leukocytes and streptococci occurred in lymph follicles. The pathologic process was analogous to the one encountered in acute infection of the pharyngeal lymphoid tissue.

PRIMARY ORBITAL MELANOMA

CASE REPORT WITH REVIEW OF THE LITERATURE

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Melanotic tumors of the orbit as a rule are secondary, arising chiefly from the uveal tract and less often from the conjunctiva, the pia-arachnoid of the brain or a more distant focus.

Carefully studied and described cases of primary orbital melanoma, with which this paper is chiefly concerned, are numerically few.

A tedious search of the world literature back to 1838, when Raimbert published his case, disclosed that most reports are brief and pathologic studies either absent or incomplete. In the accompanying table the collected reports are tabulated and brief notes of criticism given. Eleven cases from the literature are summarized in the following section.

REPORT OF CASES FROM THE LITERATURE

LAURENCE'S CASE.—A woman aged 62 had increasing proptosis until, after nine months, the eye was outside the orbit. The eye together with an intimately adherent encapsulated melanotic tumor was removed. The growth promptly recurred, filling the orbit. In six months the patient was dead. The eye was described as completely devoid of disease. The vitreous was normal, but the retina was detached.

LANGE'S CASE 1.—A woman aged 37 was well until three months before examination, when there appeared in succession pain in the left eye, proptosis and diplopia. Physical examination disclosed proptosis of 8 mm., restricted ocular movements and a nodular, nontender growth in the superior part of the orbit. Examination of the fundus disclosed congested veins. At operation there were found many small nodules, varying in size from a cherry to a hazelnut, adherent to one another and to the periosteum of the orbital roof. The growths were removed and the eye spared. The tumors were composed of round and spindle cells containing much pigment. Between the cells was a fine fibrillar tissue. The patient made a good recovery. Two years later no recurrence had taken place. Vision on the side operated on had not changed.

LANGE'S CASE 2.—A youth aged 18 years had had gradual proptosis of the right eye for one and a half years and diplopia recently. Physical examination disclosed

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unilateral proptosis of 7 mm. and a tumor palpable through the upper lid. Ophthalmoscopic examination disclosed congested vessels in the fundus. The vision was normal and the ocular movements restricted. At operation a walnut-sized, smooth, encapsulated and highly pgimented tumor, bound by adhesions to the periosteum of the roof of the orbit, was extirpated. Though the eye was spared by the operator, a postoperative infection destroyed it. Eleven and a half months later there were no evidences of metastasis. Microscopically, the following areas were seen: (1) areas composed of granulation tissue in which were spindle and stellate cells and in which pigment was present both intracellularly and extracellularly; (2) areas consisting of fibrous tissue and numerous strongly pigmented spindle cells, small and large, and (3) areas containing numerous densely packed, markedly pigmented cells and a fine fibrillar intercellular substance. The tumor was diagnosed as richly vascular melanotic fibrosarcoma.

ACHENBACH'S CASE.—A woman aged 65 had had increasing proptosis and diplopia for many months. The eye together with a retrobulbar melanotic tumor was removed. For the next year and a half the patient remained well. The outer surface of the eye was normal except in the posterior portion, where a lobulated growth 32 by 18 mm. was found fused both to the sclera and to the sheath of the adjacent optic nerve. It lay entirely within the muscle cone. At the site of fusion there was seen in the sclera a darkly pigmented linear area measuring 2 mm. The tumor was described as being richly cellular, with spindle and round cells. Much melanin pigment was present both intracellularly and extracellularly. In the pigmented linear area observed grossly, ciliary nerves were seen surrounded by cuffs of spindle and round tumor cells. The choroid and the retina were free of new growth. The author was of the opinion that the tumor arose from melanin-containing cells normally present where the ciliary nerves enter the sclera.

WALTER'S CASE.—A woman aged 48 had severe headaches and slowly progressive proptosis for six years. When she was seen by the author the eye was excessively displaced. The eye and the orbital contents were removed. A growth was found entirely within the muscle cone, partly surrounding the optic nerve. The only point of adhesion was at the apex of the orbit. The tumor measured 42 by 27 by 35 mm. and was encapsulated by tough fibrous tissue. During operation a thick gray-green fluid had escaped when the tumor was accidentally injured; on section, this was found to have come from a large cavity. Adjacent to the cavity the tumor tissue was soft and friable, while toward the periphery it was firmer and stratified. The eye muscles were intensely black and the optic nerve normal. No growth was demonstrated in the globe grossly or microscopically. Section of the tumor disclosed many spindle and round cells. Some pigment was observed in these. More pigment was demonstrated in large cells at the periphery of the growth and in the surrounding fat.

GAYET'S CASE.—The patient, a man, had a black ulcerated growth filling one orbit. The eye had been enucleated thirteen years previously because of injuries sustained in an accident. The growth had appeared one year before and had occupied the orbit gradually. Examination of the enucleated eye disclosed nothing unusual except two dark spots in the sclera. No mention of microscopic examination of these was made.

DODD'S CASE.—A woman aged 83 had a melanotic tumor of the left orbit and upper lid. It had appeared two months before in a former site, gradually increasing

Tabulation of Cases Collected from the Literature

Year	Author	Age, Yr.	Sex	History	Comment
1838	Raimbert	59	♂	Fungating orbital growth of 1 year's duration; eye and growth removed; latter promptly recurred; patient died of hemorrhage; necropsy, generalized metastasis	Eye not examined
1841	Giraldès	57	♂	Apple-sized growth in left orbit, displacing eye, 4 years' duration; growth removed, eye spared; no follow-up	Tumor inky, encapsulated and distinct from eyeball
1851	Winship	..	..	Painful swelling at external commissure of right eye developed rather suddenly; followed by slow progressive proptosis; complete removal of eye and orbital contents; tumor found in orbit loosely adherent to sclera and optic nerve	Tumor composed of tissue yellow in some areas, dark in others; no description of eye
1852	Bouisson	40	♀	Tumor filling orbit; headache; growth and eye removed; patient discharged in 3 months apparently cured; no follow-up	Eye not described; growth black, lobulated, encapsulated
1852	Lightfoot	36	♂	Proptosis and progressive loss of vision for 3 years; externally, eye looked normal; growth and tumor removed	Inside of eye not described; mass dark, resting on sclera
1853	Stoeber	..	..	See text (2 cases)	
1856	Bobbs	68	♂	Gradual loss of vision for 6 years; proptosis for 3 years; massive fungating growth filling orbit; eye and growth removed; well after 3 years	No pathologic study of eye or tumor
1864	Virchow	..	..	No clinical data	Encapsulated black growth partially encircling optic nerve; adjacent to latter, tumor perforated sclera and filled vitreous
1865	Laurence	..	..	See text	
1867	Mooren	14	..	Growth on inner orbital wall causing deviation of eye	No description of tumor or eye
1868	Sichel	37	♂	Orbital growth of 7 years' duration; eye and growth removed; no follow-up	No description of eye
1877	Waldhauer	..	..	Diminishing vision 1½ years; proptosis; eye and growth removed	No pathologic study
1880	Bennett	Adult	♂	Tumor on anterior part of orbit, displacing eye; fundus examination, negative results; growth removed, eye spared; no follow-up	Only proof that growth was primary in orbit, negative results of ophthalmoscopic examination
1881	Shakespeare	Elderly	♀	Orbital contents removed 6 months before; patient returned with orbit filled with black tumor	No pathologic study
1882	Dufail	Adult	♂	Proptosis soon after injury; eye and orbital growth removed	No description of eye
1884	Pollack	51	♂	Eye removed 10 years before for intraocular tumor diagnosed as gliosarcoma; in 4 years orbit filled with melanosarcoma	Tumor obviously primary in eye; orbital growth represented a recurrence
1886	North London University College	62	♂	Gradual loss of vision for 3 years, then blindness, proptosis and finally pain and hemorrhage from eye; eye removed; dark growth found within it; in 3 months, recurrence; other recurrences	Primary tumor of eyeball with secondary orbital recurrence
1886	Otte	20	♂	Blue-black nodule on inner angle of eye; after removal it recurred and spread rapidly; necropsy, orbit filled with growth, metastasis generalized and spread through adjacent bones to opposite side, cranium, brain	Primary site of tumor, conjunctiva

1889	Smith	29	♂	Ocular pain and loss of vision for several weeks; eye removed; in about 5 months, orbit filled with growth	No study of eye
1892	Crawford	2½	..	Fungating orange-sized growth protruding from orbit	No pathologic study
1893	Polignani	..	..	Generalized melanosarcoma with nodule in each orbit	Primary site not determined
1893	Walter	..	..	See text	
1894	Lange	..	..	See text	
1896	Achenbach	..	..	See text	
1897	Williams	40	♀	Eye removed for iridocyclitis; 4 years later, tumor mass in orbit	No examination of eye
1897	Gayet	..	..	See text	
1899	Wiesner	6½	♀	Large, ulcerated, fungating growth protruding from socket; eye and orbital growth removed; socket refilled quickly	No pathologic study described
	Wolf, cited by Wiesner	8	♂	Melanotic sarcoma of orbit; removed and recurred	No mention of eye
1901	Roselli	..	..	Pain, proptosis and gradual loss of vision to blindness; eye and mass behind it removed	Examination of eye showed tumor in choroid; despite this, author felt primary growth was in orbit
1901	Dodd, H. W.	71	♀	Orange-sized mass filling orbit and surrounding eye; tumor and eye removed	No study of eye reported
1903	Dodd, H. W.	..	..	See text	
1904	Lagrange	..	..	See text	
	Lebert, cited by Lagrange. Case 1	63	♀	Left eye blind for some time as result of inflammation; growth developed on superior aspect of globe; tumor and eye removed	On posterior aspect of eyeball was growth the size of large nut; spongy, encapsulated and pigmented; microscopic examination showed it was composed of spindle cells containing melanin pigment; tumor penetrated eyeball
	Case 2	..	..	No history	Tumor same as in case 1 except that eye was not involved
	MacKenzie, cited by Lagrange	51	♂	Vision lost in one eye 25 years before; proptosis developed; eye found pushed out of orbit by fungating growth still covered by conjunctiva; growth covered all of eye except cornea; complete exenteration	Growth encapsulated and on section appeared black as coal; composed of cells of various sizes and shapes filled with pigment granules; description of eye not given
1908	McConnell and Burman	..	..	Seven years before observation, patient discovered by accident he was blind in one eye; eye removed; four years later orbit filled with tumor	Eye not examined
1910	Haden	5	..	Proptosis; eye and tumor removed; tumor recurred several times; death in 14 weeks	No pathologic study
1911	Leeper	60	♂	Orbit filled with tumor; eye removed 1 year before because of swelling	No study made of eye
1916	Heckel	..	♂	Left eye blind 12 years; examination disclosed shrunken, soft eyeball and large black mass filling orbit; removed; mass recurred 3 times	No study of eye described
1926	Mulock	..	..	See text	
1931	Casanovas Carnicer	..	..	See text	
1937	Benedict	..	..	See text	
1940	Harbert	42	♂	Melanoma of right eye eroding through sclera and filling orbit	Definitely primary in eyeball

in size. When the patient was admitted the upper lid was swollen and drooped. It was occupied by a growth which showed blue through the skin. The eyeball was obscured from view, but its movements were free in all directions. At operation the eye and a tumor occupying the entire orbit were removed. No pathologic study is described. In the author's opinion the tumor was primary in the conjunctiva and by extending back occupied the orbit secondarily.

Lagrange's Case.—A man aged 60 was first seen in 1885 because of diminishing vision, and a diagnosis of syphilitic neuroretinitis was made. When he was seen again in 1890 no improvement was observed. In 1892 proptosis was found. Ophthalmoscopic examination disclosed a congested fundus. The proptosis increased, and the vision became worse. In January 1893 the orbital contents and the eye were removed. According to the pathologic report, an encapsulated tumor loosely adherent to the globe lay in the muscle cone encircling the optic nerve. On section the growth was seen to be intensely black and somewhat friable anteriorly and less black and less firm posteriorly. In places it was compact, fleshy and red. Histologic study disclosed irregular cells of varying sizes, some round and others polyhedral. Much pigment was present both inside and outside the cells. There is no description of the eye.

Mulock's Case.—A woman aged 55 had headache, diminishing vision and slowly progressing proptosis. Ophthalmologic examination disclosed a choked disk. A Krönlein operation was performed. A large melanotic tumor was found covering much of the eye and enveloping the optic nerve. The tumor was described as encapsulated, highly pigmented in some areas and less pigmented in others. The retina and the choroid grossly appeared normal except for a few small nodules in the outer part of the choroid which under the microscope were seen to be ciliary nerves surrounded by tumor. These in the opinion of the author and a committee formed to study the growth were extensions from the outside following the nerves and did not represent a primary choroidal neoplasm.

Casanova's Case.—A woman aged 60 had had conjunctivitis and diminution of vision for three years and progressive proptosis for one year. The globe, the tumor and the orbital contents were removed. On accidental section of the growth a dark thick fluid escaped from it. Two and a half years after operation no recurrence had taken place. The tumor was encapsulated and intensely pigmented. It partially surrounded the optic nerve. The eyeball was normal except for a small black area in the sclera continuous with the outside growth. The tumor on histologic study was found to be composed of cells of varying sizes, round and fusiform, containing different amounts of pigment granules. The pigmented area in the sclera presented a similar appearance. The choroid and the retina were normal.

Benedict's Case.—A boy 15 years of age had suffered several severe injuries to his head in early childhood, and to these was attributed a mild proptosis of four years' duration. Examination revealed discoloration of the conjunctiva, of the right side of the soft and of the hard palate and of the mucous membrane of the right naris. A specimen taken for biopsy from the lower part of the conjunctiva was reported to be stained by old blood pigment. A diagnosis of hemangioma was given, and ligation of the right carotid artery and its branches was carried out. The proptosis progressed, however, until the cornea was lost and exenteration of the orbit became necessary. All the retrobulbar orbital tissue was intensely

pigmented, and near the apex of the orbit degeneration and necrosis had extended to complete softening. There was approximately 10 cc. of thick material of the color and consistency of tar. The orbit healed in the usual time. The pathologic report stated that the tissue was deeply pigmented melanoepithelioma. Nine years later the patient was well and there had been no recurrence.

From analysis of these reports it would appear that Walter's contribution is the sole well worked up history of an example of uncomplicated primary orbital melanoma without involvement of the eye. In other cases, such as that of Casanovas, a small melanotic area was found

Fig. 1.—Frontal view of patient, showing moderate degree of proptosis.

in the sclera, while in the cases of Mulock and Achenbach melanotic cells were observed about scleral ciliary nerves. The primary orbital origin of the tumors in Virchow's and in Lebert's case can be questioned on the ground that the posterior wall of the eyeball was found to be involved by growth. Concerning other contributions, that of Harbert and that emanating from North London University College are undoubtedly reports of tumors arising in the uveal tract. So probably is Roselli's contribution despite his own opinion that the choroid was only secondarily involved. Polignani's patient appears to have had metastasis from some distant focus. In another group of cases, comprising those of Pollack, McConnell and Burman, Smith, Gayet and Leeper, the orbital

growth appeared some time after the eye had been removed. In these cases, unfortunately, the enucleated member was not subjected to pathologic study and hence a primary growth from this source could not be ruled out. When the orbital tumor occurs thirteen years after enucleation of the eye, the question of the site of genesis becomes perplexing. However, Newton reported a definite primary melanoma of the choroid removed and in thirteen years recurring in the orbit.

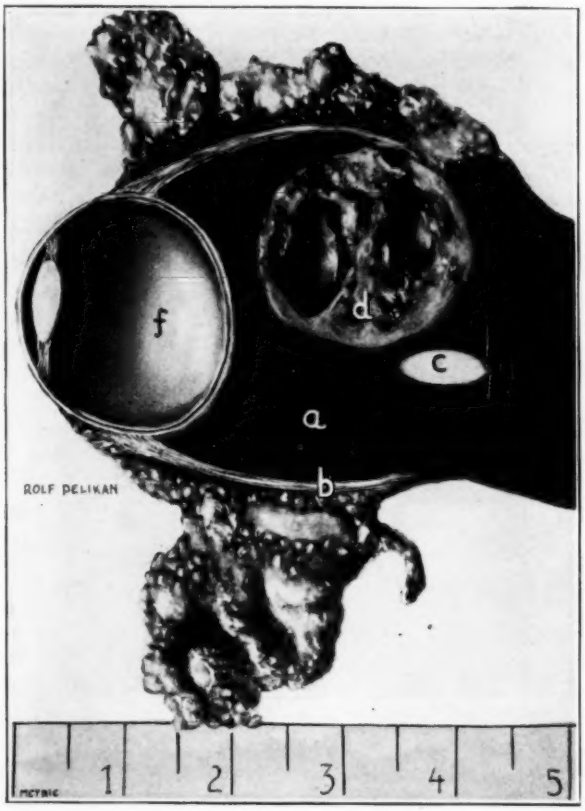

Fig. 2.—The eye and the orbital contents, sagittal section. Note the tarry mass (*a*) displacing and distending the orbital muscles (*b*), surrounding the optic nerve (*c*) and enveloping a spherical, cystic, nonpigmented tumor (*d*). The surrounding fat (*e*) is pigmented. The eyeball (*f*) appears tumor free.

Other contributions on probable primary orbital melanoma are weakened by lack of complete data. Thus Lagrange and, more recently, Benedict failed to describe the enucleated eye. The same criticism is true of Stoeber and Laurence, who stated that the eye in their cases was normal but failed to describe the degree of care with which their

study was conducted. As for Bennett and Giraldès, who were able to spare the eye after removing the tumor, their reports appeared before sufficient time had elapsed to allow a small growth in the uveal tract to become manifest. The cases of Lange were questioned as instances of true melanoma by Berlin, and Lange countered by restudying the material, redescribing it and offering drawings as proof of the correctness of his original diagnosis.

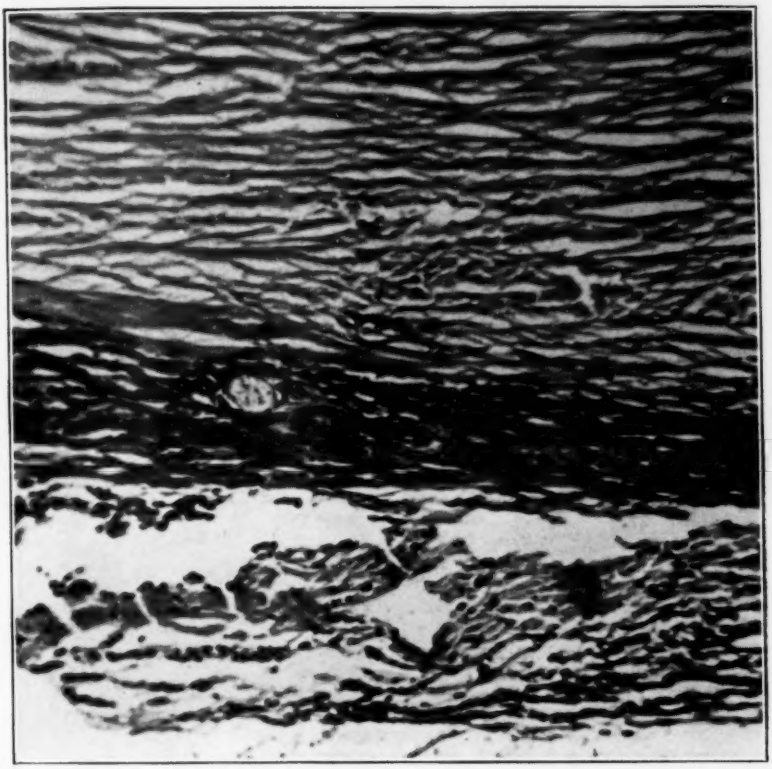

Fig. 3.—The sclera (low power magnification, hematoxylin and eosin stain) showing chromatophores in the outer third.

All the remaining reports are rendered valueless either because pathologic study is lacking or because the descriptions are poor and incomplete.

REPORT OF CASE

N. C., a white man aged 27, entered St. Vincent's Hospital on May 6, 1940 complaining of proptosis of the left eye present for five years. It had developed slowly until the past year, when it seemed to grow more rapidly. Of late, also, he had noticed some loss of vision. On physical examination the only pertinent finding pertained to the left eye, which definitely protruded (fig. 1). On palpa-

tion one could feel through the lids a soft mass evidently filling the orbit. The vision was 10/40—2 in the left eye and 10/15 in the right eye. Roentgen ray study of the skull gave negative results.

At operation, on May 16, the orbit was found to be completely filled by a tarry mass. The mass hugged the eyeball closely, making enucleation impossible.

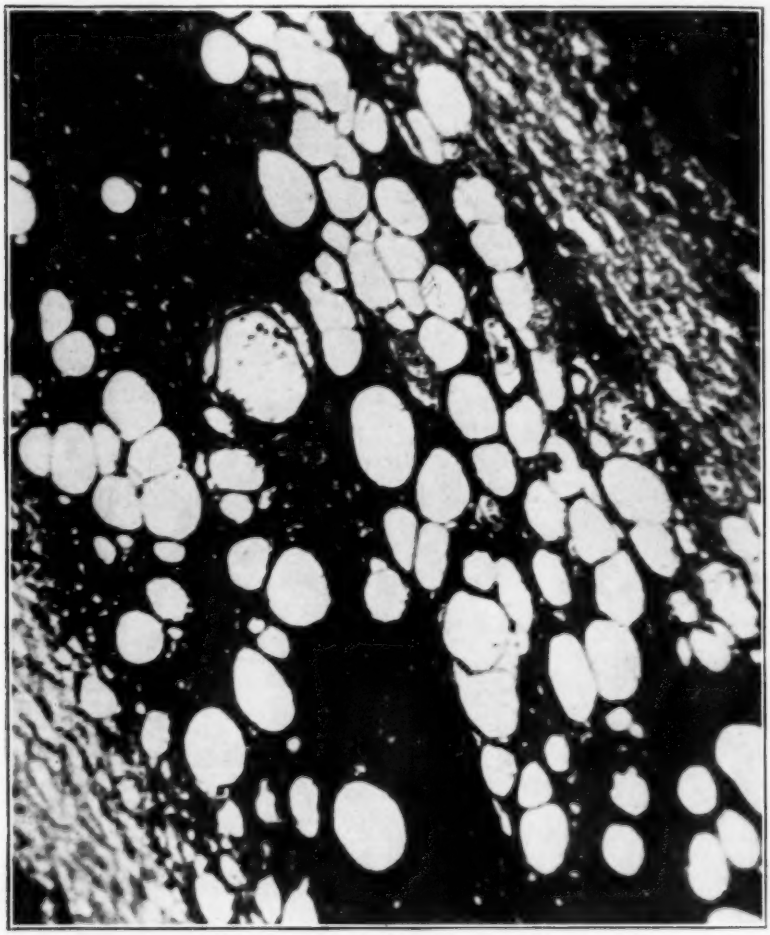

Fig. 4.—Orbital fat (low power magnification, hematoxylin and eosin stain), showing infiltration with large amounts of melanin pigment.

A complete exenteration was therefore performed. Not all the black tissue was removable, for some extended through the optic foramen into the cranial cavity. The postoperative course was uneventful. Several radium treatments were given. The orbit filled in nicely with healthy granulation tissue, and the tarry material disappeared. The patient has been wearing an artificial eye. When he was last seen, June 2, 1941, there was no evidence of recurrence or metastasis.

Fig. 5.—Perineural infiltration with melanin pigment (low power magnification, hematoxylin and eosin stain).

Fig. 6.—Orbital muscle (low power magnification, hematoxylin and eosin stain), showing melanin between the muscle fibers.

Pathologic Report.—The specimen consisted of an eye and an orbital growth measuring 5 by 5 by 4 cm. and weighing 50 Gm. (fig. 2). While the anterior half of the eye appeared free, the posterior portion was hidden from view by an enveloping tar-colored mass. On sectioning the specimen sagitally, one found the muscle cone enlarged and occupied by pitch black, firm tissue having a finely laminated appearance. Anteriorly it was fixed to the outer surface of the posterior half of the globe. Five millimeters from the eyeball, superior to the optic nerve, which channeled through the tar-colored tissue, was a firm, spherical,

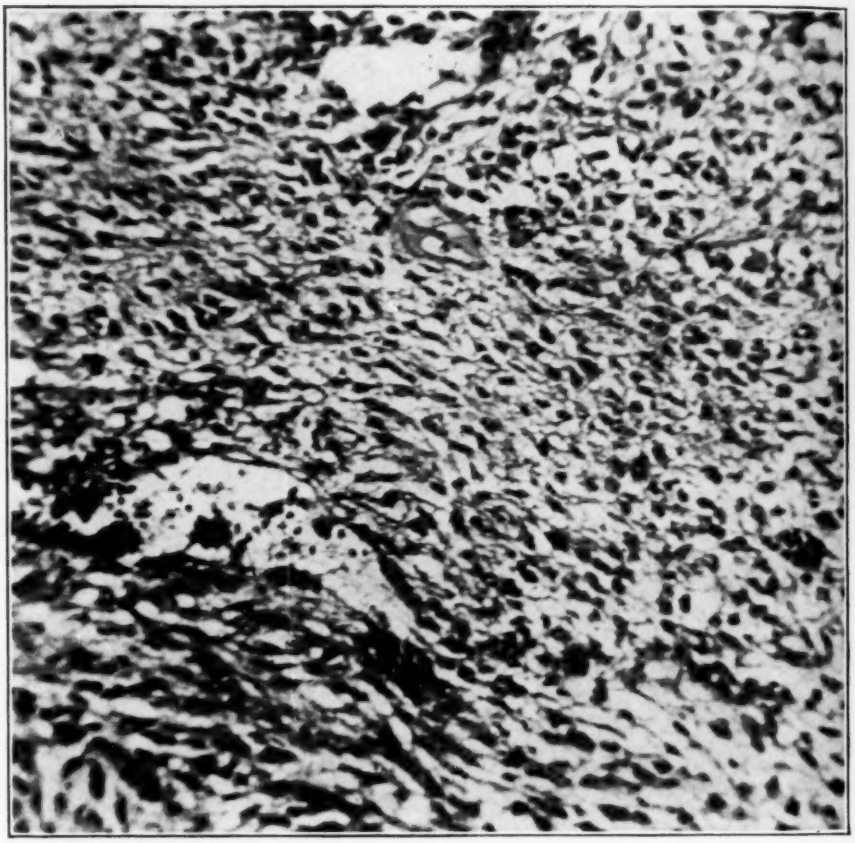

Fig. 7.—Section through the colorless part of the tumor (high power magnification, hematoxylin and eosin stain). Note the stellate appearance of the cells arranged in a reticular pattern.

gray tumor, 2 cm. in diameter, containing several irregular cysts, from which when they were sectioned fluid escaped. The eyeball itself was normal. No infiltration of its wall could be made out. The uveal tract was entirely normal. The optic muscles were stretched, thin and black. External to them, one saw adherent black, fatty tissue.

Microscopic Examination.—The entire eyeball, orbital contents and tumor were fixed in solution of formaldehyde U. S. P. in saline solution (1 : 10), cut into conveniently sized blocks and embedded in paraffin. Sections from these blocks

were prepared with hematoxylin and eosin, Masson trichrome and Foot and Foot reticulum stains.

The various components of the eyeball were found to be normal except for the sclera of the posterior half (fig. 3), where many irregular cells were found so engorged with pigment that only their outlines were recognizable.

The tarry material within the muscle cone was composed largely of melanin, free and intracellular, arranged in large dense masses infiltrating fatty, loose

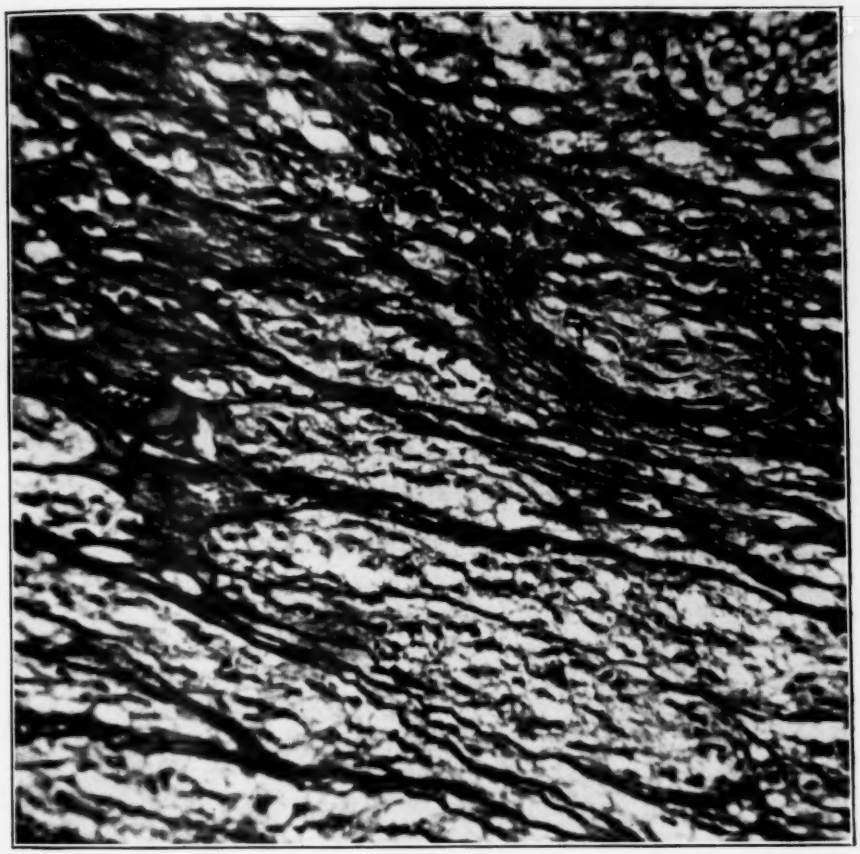

Fig. 8.—Section through the peripheral portion of the colorless tumor tissue (high power magnification, reticulum stain), showing reticulum fibers surrounding nests of tumor cells.

areolar tissue, the ciliary ganglion and the epineurium of the various nerve trunks. The same formation was seen to a lesser degree in the loose tissue between the muscle fibers (figs. 4, 5 and 6).

The colorless part of the tumor was richly cellular. In many areas the cells were spindle shaped and arranged in compact interlacing bundles. In other areas they were slightly separated and stellate, with short fine protoplasmic processes forming a reticular pattern (fig. 7). The nuclei were moderately large—oval or round—each with a prominent nucleolus, a few linin fibers and a small amount of

granular chromatin material. Cytoplasm was scant and some cells vacuolated. No cells appeared to contain melanin.

Stroma was sparse, appearing as strands of fine reticulum tending to partially or completely encircle cell bundles (fig. 8).

Blood vessels were present in moderate numbers. These were of broad caliber and lined by simple endothelium. Only an occasional one had muscle. Several vessels were thickened because of subendothelial hyalin. One channel was thrombosed.

COMMENT

The occurrence of primary orbital melanoma is so rare that it becomes necessary in each case to rule out extension from the eyeball and metastasis from a more distant focus. Thus, melanoma of the uveal tract may follow the ciliary nerves into the eye socket and there grow to large size (Friedenwald).

Achenbach and Casanovas each have reported a small primary tumor in the sclera associated with a larger orbital neoplasm. It was their belief that the scleral growth arose from melanotic cells normally present about the ciliary nerves. This conclusion, however, is open to question, since it is based on the unproved assumption that the pigmented scleral cells were melanoblasts. With regard to this assumption it must be emphasized that melanin-containing cells may be either chromatophores (macrophages) or melanoblasts and that it may be impossible to distinguish one from the other. A second ground for criticism lies in the fact that the equally plausible alternative of secondary extension into the eyeball from a primary growth in the orbit had not been ruled out. It is interesting to note at this point that an identical stand was taken by Mulock relative to the tumor cells found in the sclera in his own case. A third source of tumor lies in the conjunctiva—melanosis oculi (Doherty and Reese)—from whence on becoming malignant the growth may involve the orbit (Otte and Dodd). Beyond the eye and in the environs of the orbit, melanoma has been described as arising in the pia-arachnoid and in the nasal sinuses. From these sites it is theoretically possible for the tumor to reach the orbit. We have not, however, encountered in the literature a report of its doing so. Malignant melanoma has also been described as arising in the lacrimal caruncle and the semilunar fold. Siotto cited instances in which the tumor spread inward from the former area, necessitating exenteration of the orbit. A final possibility is metastasis to the orbit from some distant focus. Polignani's case appears to be the only example of this mode of spread. From careful study of our specimen and the history of the patient subsequent to operation, we have not been able to establish any of the conditions mentioned. Hence we are left with the sole alternative of regarding the growth as a primary orbital tumor.

We were next interested in finding the specific element from which the tumor might have arisen. G. Dvorak Theobald (1937) in a study of a series of cases of choroidal melanoma demonstrated the origin of the

growth in Schwann cells of ciliary nerves, thus lending support to the neurogenic theory. Search on our part to find such cells in the extraocular course of these or other orbital nerves was unsuccessful. We were able to dispense with epithelial elements as the source of the tumor, since the lacrimal gland, the only orbital source of epithelium, was normal. No attempt to elaborate on Ribbert's theory of a mesoblastic origin of melanoma will be made, because this theory has been discussed amply by others (e. g. Ewing) and, furthermore, we have nothing new to add.

Of prime concern in our case is the question of the degree of malignancy. Satisfactory reports of primary orbital tumors are too few to enable one to speak with authority on this point. However, in view of the behavior of melanoma in other portions of the body, one must assume a guarded position despite the fact that the tarry material left behind at operation in our case regressed and to date no recurrence or metastasis is evident. It is well known that choroidal tumor may not recur for ten or more years (Newton).

Of interest in our case is the puzzling relationship between the two types of tissue constituting the tumor. One was centrally located, colorless, cystic and composed of nonpigmented spindle and stellate cells, while the other consisted in reality of normal orbital contents enlarged to tumor proportion by massive and diffuse infiltration with cells packed with pigment. This infiltration gave to it a pitch black color and firm consistency. Further study revealed that it could readily be peeled off both from the eyeball and from the colorless part of the tumor, a circumstance indicating lack of continuity and of close relationship between the two parts. It is our opinion that the majority of the cells constituting the black part of the growth were chromatophores (macrophages) rather than neoplastic melanoblasts.

SUMMARY AND CONCLUSIONS

1. A case of primary orbital melanoma is reported.

2. A review of the literature disclosed (*a*) that the orbit as a source of melanoma is rare; (*b*) that most of the reported cases are instances of melanoma secondary to growth in the uveal tract, conjunctiva, etc., and (*c*) that cases which might be acceptable as instances of primary orbital melanoma were incompletely studied and described.

NOTE.—The patient was last seen on April 29. He had remained well, with no evidence of recurrence.

BIBLIOGRAPHY

Achenbach, W. C.: Ein Fall von orbitalem Melanosarcom ausgehend vom episcleralen Gewebe hinter dem Bulbus, Virchows Arch. f. path. Anat. **143**:324-332, 1896.

Benedict, W. L.: Clinical Considerations of Melanotic Neoplasms of the Eye and Orbit, Surg., Gynec. & Obst. **64**:513-516, 1937.

Bennett, E. H.: Melanotic Sarcoma of the Orbit, Dublin J. M. Sc. **70**:66-67, 1880.

Berlin, R.: Das Melanosarcom der Orbita, in Graefe, A., and Saemisch, E. T.: Handbuch der gesammten Augenheilkunde, Leipzig, Wilhelm Engelmann, 1880, vol. 6, p. 713.

Bobbs: Melanotic Tumor of the Orbit, Tr. Indiana M. Soc. **7**:27-30, 1856.

Bouisson: Mémoire sur l'opération souscutanée des tumeurs [case 3], Arch. gén. de méd. **29**:24, 1852.

Casanovas Carnicer, J.: Contribución al estudio anatomo-patológico de los melanomas orbitarios, Arch. de med., cir. y especialid. **34**:659-661, 1931.

Crawford, D. H.: Melanotic Sarcoma of Orbit, Indian M. Gaz. **27**:295, 1892.

Dodd, H. W.: Removal of All the Contents of the Orbit for Malignant Growth, M. Press & Circ. **72**:547, 1901.

Removal of Melanotic Sarcoma of the Orbit, ibid. **77**:331, 1903.

Doherty, W. B.: Cases of Melanosis Oculi with Microscopic Findings, Am. J. Ophth. **10**:1-7, 1927.

Dufail, P.: Des sarcomes de l'orbite et de leur traitement par l'extirpation des parties molles, Thesis, Paris, no. 48, 1882, pp. 78-79.

Ewing, J.: Neoplastic Diseases, ed. 4, Philadelphia, W. B. Saunders Company, 1940, p. 949.

Foot, C.: Concerning the Histology of Melanoma, Am. J. Path. **8**:309-319 and 321-327, 1932.

Friedenwald, J. S.: The Pathology of the Eye, New York, The Macmillan Company, 1929, p. 294.

Gayet: Tumeur de l'orbite, Ann. d'ocul. **117**:288, 1897.

Giraldès: Tumeur mélanique de l'orbite, Ann. chir. franç. et étrang. **3**:232-238, 1841.

Haden, J. B.: Melanotic Sarcoma of the Orbit, Ophth. Rec. **19**:24-25, 1910.

Harbert, F.: Malignant Melanoma of the Orbit, U. S. Nav. M. Bull. **38**:378-380, 1940.

Heckel, E. B.: Report of a Case of Melanosarcoma of the Orbit Treated with Radium, Arch. Ophth. **45**:465, 1916.

Lagrange, F.: Traité des tumeurs de l'oeil, de l'orbite et des annexes, Paris, G. Steinheil, 1904, vol. 2, pp. 436-446.

Lange, O.: Zur Casuistik der Orbitaltumoren, St. Petersburg med. Wchnschr. **6**:325, 1881.

Zwei Fälle von Melanosarcom der Orbita, Klin. Monatsbl. f. Augenh. **32**:61, 1894.

Laurence, J. Z.: Melanotic Tumour of Orbit, Tr. Path. Soc. London **16**:235-236, 1864-1865.

Lebert, H.: Cancer mélanique du pourtour de l'oeil, in Traité d'anatomie pathologique, générale et spéciale, Paris, J. B. Baillière & fils, 1857, vol. 1; cited by Lagrange.

Leeper, B. C. A.: Case of Melanotic Sarcoma Primarily Affecting the Orbit with Secondary Deposits in Pleura, Liver and Lungs, Lancet **1**:937, 1911.

Lightfoot, R. T.: Melanotic Tumor of the Orbit Unconnected with the Eyeball, M. Times, London **5**:248, 1852.

McConnell, G., and Burman, R.: Report of a Case of Melanosarcoma of the Orbit, Boston M. & S. J. **159**:108-111, 1908.

MacKenzie, W.: Traité pratique des maladies de l'oeil, traduit de l'anglais avec notes et additions par S. Laugier et par G. Richelot, Paris, B. Dusillon, 1844, p. 486; cited by Lagrange.

Masson, P.: Les naevi pigmentaires, tumeurs nerveuses, Ann. d'anat. path. **3**:417-453, 1926.

Melanotic Sarcoma of Orbit, North London or Univ. Coll. Hosp. Rep. (1885), 1886, pp. 26-27.

Mooren, A.: Ophthalmiatrische Beobachtungen, Berlin, A. Hirschwald, 1867, p. 34.

Mulock, A. W.: Discussion of Intraocular and Extraocular Melanomata, Tr. Ophth. Soc. U. Kingdom **46**:122-127, 1926.

Newton, F. R.: Local Recurrence of Melanoma of Choroid Thirteen Years After Enucleation, Am. J. Ophth. **21**:668, 1938.

Otte, R.: Ein Fall von melanotischem Sarkom der rechten Orbita mit Uebergang auf die benachbarten knöchernen, Theile des Schädels, Halle, Germany, C. A. Kaemmerer u. Comp., 1886, pp. 1-30.

Polignani, L.: Noduli di melanosarcoma metastatici nei muscoli estrinseci dell'occhio, Naples, A. Tocco, 1893.

Pollack: Melanosarcoma of Orbit, St. Louis M. & S. J. **46**:153-156 and 269-270, 1884.

Raimbert: Tumeur encéphaloïde mélaïnée développée dans l'orbite, Bull. Soc. anat. de Paris **13**:193-195, 1838.

Reese, A. B.: Precancerous Melanosis and Diffuse Malignant Melanoma of the Conjunctiva, Arch. Ophth. **19**:354-365 (March) 1938.

Roselli, R.: Melano-sarcoma retrobulbare dell'orbita destra, Boll. d. r. Accad. med. di Roma **27**:256-265, 1901.

Schnitker, M. T., and Ayer, D.: Primary Melanoma of Leptomeninges, J. Nerv. & Ment. Dis. **87**:45-73, 1938.

Shakespeare: Melanotic Sarcoma of the Orbit with Metastasis to the Liver, Tr. Path. Soc. Philadelphia (1881-1883) **40**:236, 1884.

Sichel, J.: Observation de tumeur encéphaloïde et mélanique de l'orbite gauche, Ann. d'ocul. **60**:18-25, 1868.

Siotto, G.: Melanoma della caruncola lacrimale, Rassegna ital. d'ottal. **7**:178-190, 1938.

Smith, A. T.: Primary Melanoma of Nasal Cavity, Arch. Otolaryng. **29**:437-445 (March) 1939.

Smith, E.: Melanotic Sarcoma of the Orbit, Physician & Surgeon **31**:546, 1889.

Stoeber: De la nature cancéreuse de la mélanose de l'oeil, Ann. d'ocul. **30**:264, 1853.

Terry, T. L., and Johns, J. P.: Uveal Sarcoma, Am. J. Ophth. **18**:903, 1935.

Theobald, G. D.: Neurogenic Origin of Choroidal Sarcoma, Arch. Ophth. **18**: 971-997 (Dec.) 1937.

Virchow, R.: Die krankhaften Geschwülste, Berlin, A. Hirschwald, 1864-1865, vol. 2, p. 279.

Waldhauer: Tumoren des Auges und der Augenhöhle [case 5], St. Petersburg med. Wchnschr. **2**:367, 1877.

Walter, O.: Ein Fall von primären Melanosarkom der Orbita, Klin. Monatsbl. f. Augenh. **31**:357-369, 1893.

Wiesner, D. H.: A Case of Melanotic Sarcoma of the Orbit in a Girl Six Years Old, Internat. J. Surg. **2**:76-78, 1899.

Williams, R.: Melanotic Sarcoma of the Orbit, Tr. Ophth. Soc. U. Kingdom **17**:243-245, 1897.

Winship: Melanotic Tumor of Orbit Unconnected with the Eyeball, Newcastle Gateshead Path. Soc. Communicat., 1851-1852, pp. 5-7.

Wolfe, cited by Wiesner.

MECHANISM OF ACCOMMODATION

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The Helmholtz [1] theory of accommodation appeared in 1855, and since that time the refutation or substantiation of this hypothesis has concerned students of ocular physiology. The difficulty of observing the interior of the anterior segment without mutilating the eye has permitted the theory to persist in explanations of this ocular function.

There are two firmly entrenched schools of thought on the mechanism of accommodation: One supports Helmholtz, and the other favors the Tscherning [2] theory. The two agree that the fundamentals of accommodation are contraction of the ciliary muscle and increased convexity of the crystalline lens but differ on the method by which the former accomplishes the latter. The followers of Helmholtz believe that contraction of the ciliary muscle reduces zonular tension, permitting the elastic capsule of the lens to shape the lens. In opposition, Tscherning's disciples think the force of the ciliary muscle acting through the zonule and the vitreous forcefully molds a relatively plastic lens into the accommodated form.

There are other theories for the mechanism of accommodation, but when one considers the fundamental question of whether the increased dioptric power of the lens results from an intrinsic property of the lens or from extrinsic pressure on that structure they may be classified as modifications of either the Helmholtz or the Tscherning hypothesis. Henderson,[3] for example, disapproved of the implication in the Helmholtz theory that the choroid must sustain the elastic traction of the lens but agreed that the lens becomes more convex through intrinsic forces. He thought that the traction of the lens is borne chiefly by the radial and the longitudinal portion of the ciliary muscle. During accommodation the tension on the zonule and the lens is released, not by the choroid's being dragged forward but by relaxation of the radial and

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1. Helmholtz, H.: Ueber die Accommodation des Auges, Arch. f. Ophth. (pt. 2) **1**:1, 1855.

2. Tscherning, M.: The Mechanism of Accommodation, Ophth. Rev. **23**:95, 1904.

3. Henderson, T.: The Mechanism of Accommodation and the Comparative Anatomy of the Ciliary Region, Ophthalmoscope **10**:502 (Sept.) 1912.

contraction of the circular muscle fibers. The longitudinal fibers have a passive role and merely prohibit stress from affecting the choroid.

Johnson [4] hypothesized that on contraction of the ciliary muscle the incompressible aqueous in the circumlental space of Petit is forced against the equator of the lens, causing the anterior and the posterior surfaces of the lens to bulge.

Stilling's [5] idea that the lens is squeezed by a ring of vitreous on contraction of the ciliary muscle followed Tscherning's line of thought.

Practically all the experimental data on this problem have been interpreted by both sides as substantiation of their respective theories. At least, neither the Helmholtz nor the Tscherning theory has been conclusively eliminated by experimental findings. The work of Hensen and Voelckers,[6] for example, has been cited by both sides to support their views. These workers cut a scleral window in the eyes of dogs to expose the ciliary muscle, and on stimulation of the ciliary nerves they saw the muscle sink inward while the exposed choroid simultaneously bulged outward. A definite shortening of the ciliary muscle was not demonstrated. Through a more posterior scleral window they saw the choroid move forward and confirmed that observation by inserting needles through the sclera into the choroid and seeing the outer ends of the needles move backward during stimulation of the ciliary nerves. They found that the choroid moved forward 0.5 mm. at the equator and the displacement diminished posteriorly. The retina was seen to move forward when a window, made through the coats of the eyeball, permitted the interior of the opposite side to be observed. After completely bisecting the globe, they found that on excitation of the ciliary nerves the part of the vitreous nearest the lens bulged forward while the periphery of the vitreous sank inward. With the lens removed, the patellar fossa bulged forward on stimulation of the ciliary nerves and receded at cessation of the stimulus. They were unable to see motion of the ciliary processes during accommodation but saw a slight forward movement of the zonule. They thought their findings substantiated the Helmholtz theory and interpreted the forward movement of the choroid as certain evidence of zonular relaxation. The opposition believed that the forward movement of the choroid and vitreous indicated that the vitreous was forced against the lens to mold its shape.

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4. Johnson, L.: A New Theory of Accommodation, Arch. Ophth. **53**:426 (Sept.) 1924.

5. Stilling, J.: On the Mechanism of Accommodation, translated by T. H. Butler, Ophthalmoscope **10**:519 (Sept.) 1912.

6. Hensen, V., and Voelckers, C., cited by Luedde, W. H.: Hensen and Voelckers' Experiments on the Mechanism of Accommodation: An Interpretation, Tr. Am. Ophth. Soc. **25**:250, 1927.

Grossmann [7] rapidly froze and sectioned atropinized cat eyes. He found the anterior surface of the lens to be regularly spherical and more strongly curved than the posterior surface. The posterior surface in many eyes showed a central flattening. Eyes frozen and sectioned while under the influence of physostigmine showed the curvature of the central part of the anterior surface of the lens to be approximately the same as in eyes under the influence of atropine, but the periphery of that surface had an increased curvature. The posterior surface showed a lenticonus but only in horizontal sections. No decrease in the equatorial diameter of the lens was found. To conform with the Helmholtz theory, Grossmann explained the cylindric curvature by assuming that greater relaxation occurred on one side of the zonule because of a corresponding difference in size in the ciliary body. Von Pflugk [8] found that monkey and pigeon eyes rapidly frozen while under the influence of physostigmine showed compression of the lens periphery with increased axial convexity. His work has been cited as evidence of compression of the lens by the vitreous. It also substantiates the findings of Tscherning [9] and others who have shown an increased curvature in the central portion of the lens surfaces by studies of Purkinje-Sanson images. Pflugk's experiments were repeated by Fischer,[10] who concluded that the freezing method is not suitable for the purpose.

Elasticity of the lens capsule was demonstrated by Helmholtz,[1] who exposed the lens and the zonule from the front and made traction with two fine forceps grasping the lens at opposite sites. The lens elongated in the direction of traction and returned to its curved shape at cessation of the pull. Lindsay Johnson,[4] to show that the lens capsule of an unaccommodated eye is not flattened by traction of the zonule, cut the lens capsule in rabbit eyes, and the capsule failed to gape. To replace the Helmholtz theory, he presented the theory of accommodation previously mentioned. Fincham [11] suspended the extirpated lens of a sheep by the zonular fibers and demonstrated the elastic recoil of the system after the lens was forcibly displaced. The object of the experiment was to prove that the zonule is a system of extensible fibers and will allow the lens capsule to constrict during accommodation. He stated the belief that the elastic properties of the lens are in the capsule, because lenses

7. Grossmann, K.: Further Investigations on Accommodation, Ophth. Rev. **23**:347, 1904.

8. von Pflugk, A., cited by Luedde, W. H.: The Mechanism of Accommodation, Tr. Sect. Ophth., A. M. A., 1931, p. 357.

9. Tscherning, M.: Changements optiques de l'oeil pendant l'accommodation, Arch. de physiol. **7**:158, 1895.

10. Fischer, F.: Ueber Fixirung der Linsenform mittels des Gefriermethode, Arch. f. Augenh. **56**:342, 1907.

11. Fincham, E.: The Mechanism of Accommodation, Brit. J. Ophth., 1937, supp. 8, p. 5.

removed from young monkey eyes lost the convexity of accommodation when the capsule was removed. Salzmann and Seeburger [12] were unable to find true elastic tissue fibers in the human lens. Von Pflugk [13] found that the elasticity of the zonule was approximately nine times as great as that of the lens capsule and concluded that the zonule has little to do with changes in the shape of the lens.

Studies of the mechanism of accommodation in the human eye have given support to both schools of thought. Grossmann [14] recorded the following changes in an aniridic eye under the influence of physostigmine: a decrease in the diameter of the lens equator; an increase in the axial diameter of the lens; an accommodative lenticonus, as shown by retinoscopic examination and study of Sanson-Purkinje images; an upward and inward shift of the lens; a narrowing of the ring of ciliary processes which never touch the lens, and trembling of the lens at the height of the effect of physostigmine. The observations by Fincham [11] in a case of aniridia were similar to those of Grossmann; but, instead of the posterior pole of the lens moving backward more than the anterior pole moved forward, Fincham found the reverse to be true. He also noted that radial striae in the zonule which were clearly visible in the unaccommodated state almost disappeared on accommodation. With the slit lamp he saw the internal parts of the lens assume changes in shape corresponding to the increase in curvature in the surfaces of the lens. He thought this indicated that the power of accommodation does not lie entirely in the cortex and that nuclear sclerosis could account for presbyopia. Duane [15] had said that partisans of the Helmholtz theory could not attribute presbyopia to nuclear sclerosis if the lens cortex remained soft. Fincham and Grossmann both stated the belief that their findings indicate relaxation of the zonule during accommodation, with a resultant increase in convexity of the lens.

The cornea and iris were removed from the freshly enucleated eye of an 11 year old child by Fincham,[11] and a picture was taken of a slit lamp beam making a sagittal section through the lens. The picture was repeated after the zonule was cut and the eye bisected at the equator to negate any effects that the vitreous might have on the lens. The pictures showed that the central part of the anterior surface of the lens had changed its radius of curvature from 12 to 5 mm., while the curvature of the peripheral part of the surface had not changed. Fincham attributed the conoid shape to variation in the thickness of the lens capsule and

12. Salzmann and Seeburger, cited by Luedde.[30]

13. von Pflugk, A.: Neue Wege zur Erforschung der Lehre von der Akkommodation, Arch. f. Ophth. **128**:179, 1932.

14. Grossmann, K.: The Mechanism of Accommodation in Man, Ophth. Rev. **23**:1, 1940.

15. Duane, A.: Accommodation, Arch. Ophth. **5**:1 (Jan.) 1931.

expressed the opinion that this change in curvature was enough to account for all the accommodation of the child. Heine [16] previously had shown that in a dead eye the convexity of the lens increased when the zonule was cut, but Tscherning [17] denied that the effect was great enough to account for accommodation.

Graves [18] reported a unique case in which the entire lens except the capsule had been absorbed. With the eye under the effect of atropine the capsule surfaces were flat and almost approximated, but with physostigmine they were separated and bulged. He pictured the central area of the anterior capsule as steeply convex and surrounded by a wide concave furrow. This contour was uniform and definite, while the posterior capsule fell into loose folds. Partisans of both sides interpreted these findings in terms of their respective theories. One side believed that the shape of the lens capsule under the influence of physostigmine is due to elastic properties of the capsule, and the other held the vitreous responsible.

Duane [15] found the loss of accommodation between the ages of 10 and 20 to be considerable and stated the belief that it is incommensurate with the probable reduction in elasticity of the lens capsule. He pointed out that a man 32 years of age had 9 D. of accommodation which fluctuated considerably. According to the Helmholtz theory he should have had 9 D. of latent accommodation and be able to maintain the maximum at all times. Homatropine, which gradually paralyzes the ciliary muscle, reduced the accommodation as fast in a man of 40, who should have had 10 to 12 D. of reserve power, as in a child 10 years old, who had much less reserve. Duane stated that these findings are inexplicable if the ciliary muscle maintains its power through middle age and acts according to the Helmholtz theory.

Hess [19] demonstrated that at the height of accommodation the lens trembled on movements of the eye and fell with gravity. The observation implied that the zonular tension was relaxed.

In a patient with a dislocated lens, W. H. Luedde [20] found that the lens moved away from the defective sector of the zonule after the instillation of pilocarpine. He thought the vitreous was forced over the edge of the lens where the zonule was defective and moved the lens in the opposite direction. In previous studies he had found that in monkey and human eyes sectioned while under the influence of atropine there was a space between the anterior limiting membrane of the vitreous and

16. Heine, L., cited by Stilling.[5]

17. Tscherning, M., cited by Stilling.[5]

18. Graves, B.: Change of Tension on the Lens Capsule During Accommodation and Under the Influence of Various Drugs, Tr. Am. Ophth. Soc. **23**:184, 1925.

19. Hess, C., cited by Fincham.[11]

20. Luedde, W. H.: Indication for the Use of Pilocarpine in Dislocation of the Crystalline Lens, Tr. Am. Ophth. Soc. **23**:71, 1925.

the posterior surface of the lens periphery and the zonule. In eyes under the influence of physostigmine the space was obliterated. This indicated a movement of the periphery of the vitreous against the zonule and the posterior surface of the equatorial zone of the lens.

F. W. Luedde [21] described a patient with a subluxated lens in whom marked iridodenesis was evident during distant vision but absent at near vision. During maximum accommodation, the iridodenesis again was noted, but to a lesser degree. This finding was interpreted as evidence of zonular tension during accommodation and certain proof of a fallacy in the Helmholtz theory.

The differences of opinion on the mechanism of accommodation result because the pieces of the puzzle are lacking which will connect the known but isolated facts to form a definite pattern. The Helmholtz partisans believe that on contraction of the ciliary muscle, the posterior end of the ciliary body and the choroid are pulled forward, allowing the zonule to relax and permitting the lens capsule to shape the lens. On maximal contraction of the ciliary muscle, the diameter of the ciliary corona is so diminished that relaxation of the zonular fibers is too great to be balanced by the elasticity of the lens capsule. Therefore, during the greatest accommodative effort, the lens trembles and sinks with gravity. The longitudinal muscle fibers draw the flat portion of the ciliary body and the choroid forward while the circular fibers pull the ciliary processes toward the lens. The conoid shape of the accommodated lens, shown by catoptric phenomena and evidence provided by eyes frozen while under the influence of physostigmine, results from a corresponding distribution of elastic tissue in the lens capsule.

The Tscherning disciples, from their interpretation of much of the experimental evidence cited by the opposing school, conclude that contraction of the radial and the meridional ciliary muscle fibers pulls forward the posterior part of the ciliary body, the choroid and the anterior peripheral portion of the vitreous. The lens periphery is compressed between the anterior capsule, which is being drawn backward by zonular traction, and the posterior capsule, which is pushed forward by the vitreous. The result is increased convexity and the conoid shape of the accommodated lens. The tremulousness of the lens and its tendency to fall with gravity during maximal accommodation were explained by W. H. Luedde.[6] He said that maximal accommodation results in contraction of the circular portion of the ciliary muscle, which releases the lens from the active support of the short suspensory zonular fibers, but the long zonular fibers keep the vitreous compressed against the lens, permitting the lens to tremble with the movement of the eye as would a

21. Luedde, F. W., cited by Luedde, W. H.: What Subluxated Lenses Reveal About the Mechanism of Accommodation, Am. J. Ophth. **24**:40 (Jan.) 1941.

bead on a mound of jelly. That the lens becomes more spherical when freed of its zonular attachments he explained by the fact that all fluid or semifluid bodies assume a spherical shape when surrounded by uniform pressure.

EXPERIMENTS

The purpose of this work was twofold: to describe a new method for observing morphologic changes in the interior of the intact eye during accommodation and to obtain information on the mechanism of accommodation in the cat.

The method employed was to make cat eyes radiopaque by the intraocular injection of a colloidal suspension of thorium dioxide (thorotrast) [22] and to take roentgenograms of the eyes while they were under the influence of a cyclotonic [23] or a cycloplegic. One-tenth cubic centimeter of the contrast medium was injected into the vitreous with a hypodermic needle inserted through the sclera approximately 8 mm. posterior to the superior limbus. During the injection the point of the needle was observed with an ophthalmoscope. Immediately afterward a paracentesis was done, and 1 drop of 0.2 per cent scopolamine hydrochloride solution was instilled onto the cornea twice daily for one week. Fragmentation and distribution of the colloidal thorium dioxide were followed by ophthalmoscopic studies and roentgenograms of the cats' heads made at intervals varying from one week to eighteen months after the injection. When the intraocular distribution of the contrast medium was satisfactory, stereoscopic roentgenograms of the isolated but living eye were made. The cat was anesthetized by the intraperitoneal injection of pentobarbital sodium solution (1 grain [0.06 Gm.] per cubic centimeter), 1.3 cc. per 5 pounds (2.3 Kg.) of body weight. A frontotemporal skin and muscle flap was made, and the bones forming the frontal sinus and the lateral and the inferior orbital margins were removed with rongeurs (fig. 1). With the exception of the extraocular muscle cone and its contents, the eye was freed of attachments. Dental films were placed under the eye on the orbital floor and roentgenograms made while the cat's head was fixed and the eye was held in the primary position. The x-ray tube was placed 24 inches (61 cm.) above the eye, and steroscopic roentgenograms were taken at 15 and at 5 degrees posterior to the plane of the iris and at 10 degrees anterior to that plane.

Roentgenograms were taken of eyes fifteen minutes after the last corneal instillation of one of the following solutions: (1) 1 per cent physostigmine salicylate, 1 drop, every ten minutes for two hours; (2) 1 per cent physostigmine salicylate and 1 per cent pilocarpine nitrate, 1 drop each, three hours before the roentgenogram and every ten minutes for nine times just preceding it; (3) 1 per cent physostigmine salicylate and 10 per cent mecholyl (acetylbetamethylcholine hydrochloride), 1 drop each, every ten minutes for ninety minutes; (4) 1 per cent physostigmine salicylate, 1 per cent pilocarpine nitrate and 1.5 per cent carbaminoylcholine chloride, 1 drop each, every two hours for ten hours, and (5) 1 per cent atropine sulfate, 1 drop every two hours for ten hours. To compare the interior of an eye under the influence of a cyclotonic with that of the same eye under the influence of a cycloplegic, roentgenograms were made of the eye after instillation

22. Thorotrast, report of the Council on Pharmacy and Chemistry, J. A. M. A. **99**:2183 (Dec. 24) 1932.

23. Used as an antonym of cycloplegic.

of one of the first four medications; then 1 per cent atropine sulfate solution, 2 drops every ten minutes, was given for seventy-five minutes and the roentgenograms repeated. In some cases the atropine was supplemented with 2.3 per cent epinephrine bitartrate solution instilled simultaneously, 1 drop every ten minutes for seventy-five minutes. All the drugs used except the epinephrine bitartrate were in a 1:5,000 zephiran [24] solution, as advocated by O'Brien and Swan [25] for enhancement of corneal penetration.

The size of the pupil was the criterion of the effect of the drug, the untreated eye acting as a control. In most of the eyes treated with cyclotonics the pupil was a vertical black line at the time the roentgenograms were taken, whereas in the eyes treated with cycloplegics the pupil had a diameter of at least 12 mm.

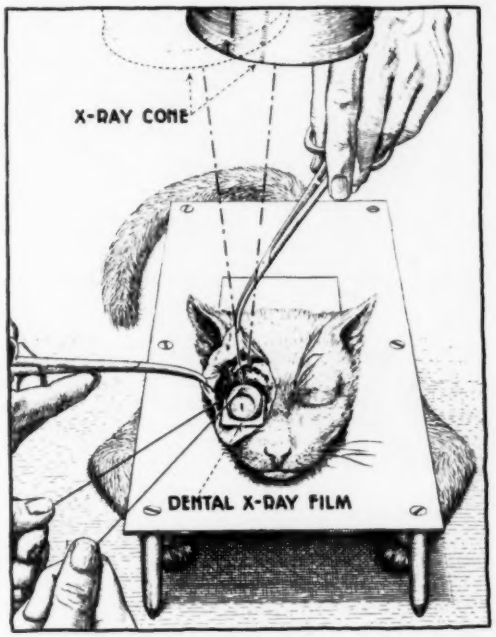

Fig. 1.—Method for taking roentgenograms of cat eyes.

Thirty cats were used; the first 20 were needed in the establishment of the technic. From studies and measurements of the best roentgenograms of the remaining 10 cats, composite stereoscopic drawings of eyes under the influence of cyclotonics and then of cycloplegics were made.

In order to correlate the details of the roentgenograms with the anatomic distribution of colloidal thorium dioxide, several eyes of which roentgenograms

24. Zephiran is a mixture of alkyl, dimethyl and benzyl ammonium chlorides. It is a cationic detergent having about the same consistency and physical properties as liquid soap, which is an anionic detergent.

25. O'Brien, C. S., and Swan, K. C.: Carbaminoylcholine Chloride in the Treatment of Glaucoma Simplex, Arch. Ophth. **27**:253 (Feb.) 1942.

were made were dissected under a microscope immediately after enucleation or after fixation in solution of formaldehyde. The eyes not so examined by roentgenogram were fixed in Zenker's solution, sectioned and studied microscopically.

RESULTS

Stereoscopic roentgenograms were obtained on which the ciliary processes, iris, filtration angle, lens and vitreous of the intact living eye were outlined. On a few films a shadow thought to be Schlemm's canal was seen. Definite divisions in the vitreous were evident; the portion anterior to the ora serrata was separated from the more posterior portion by distinct borders. In deference to the embryologists, the anterior

Fig. 2.—Section of a cat eye showing thorium dioxide–laden phagocytes in the meshwork, in the iris root and in Schlemm's canal.

portion of the vitreous was considered tertiary, and the posterior, secondary vitreous. A few films showed a shadow that was probably the primary vitreous. The tertiary vitreous was bounded anteriorly by the zonule, posteriorly by the secondary vitreous and centrally by the lens and the primary vitreous. The retina formed the posterior boundary of the secondary vitreous, while anteriorly it contacted the tertiary vitreous. The primary vitreous appeared to be a cone extending from Egger's line to the optic disk. The temporal side of the ciliary body was identified by its wide orbicular portion, the nasal side having practically no orbiculus ciliaris.

Dissection of eyes containing colloidal thorium dioxide and fixed in solution of formaldehyde showed a white pseudomembrane coating the

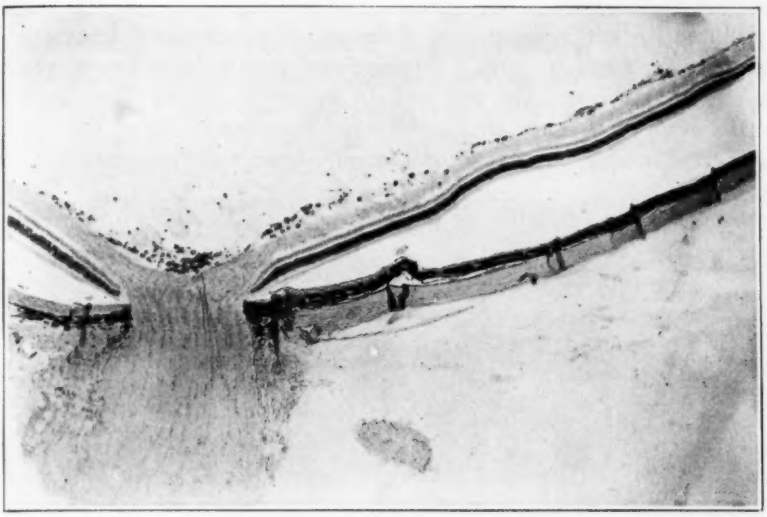

Fig. 3.—Section showing thorium dioxide–laden phagocytes on the optic disk and the retina.

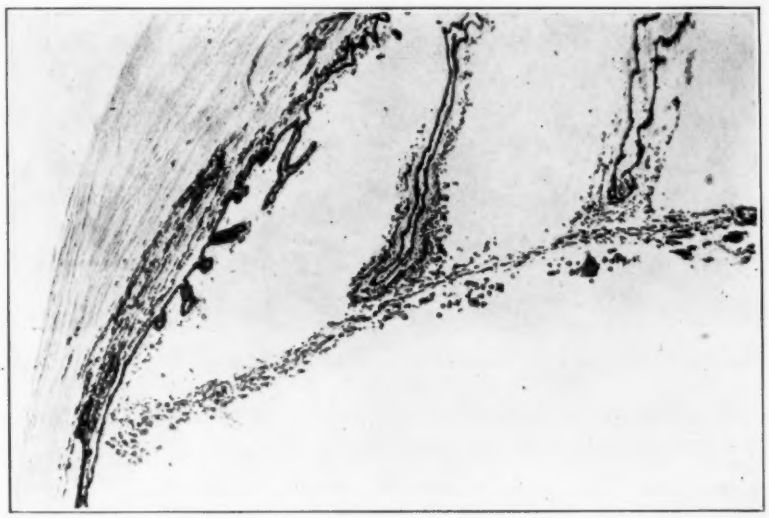

Fig. 4.—Section showing thorium dioxide–laden phagocytes on the ciliary processes and the anterior part of the hyaloid membrane.

ciliary epithelium. Just anterior to the ora serrata it turned axialward and blended with a more delicate, but similar, pseudomembrane which attached at the ora serrata. The effects of the fixative on the vitreous prohibited further investigation of the pseudomembrane. After the eye had dried for a few minutes, a white granular material was seen covering the ciliary epithelium, the lens and the meshwork of the filtration angle.

Bisection of freshly enucleated eyes revealed a white film on the ciliary epithelium. It extended centrally from the posterior portion of

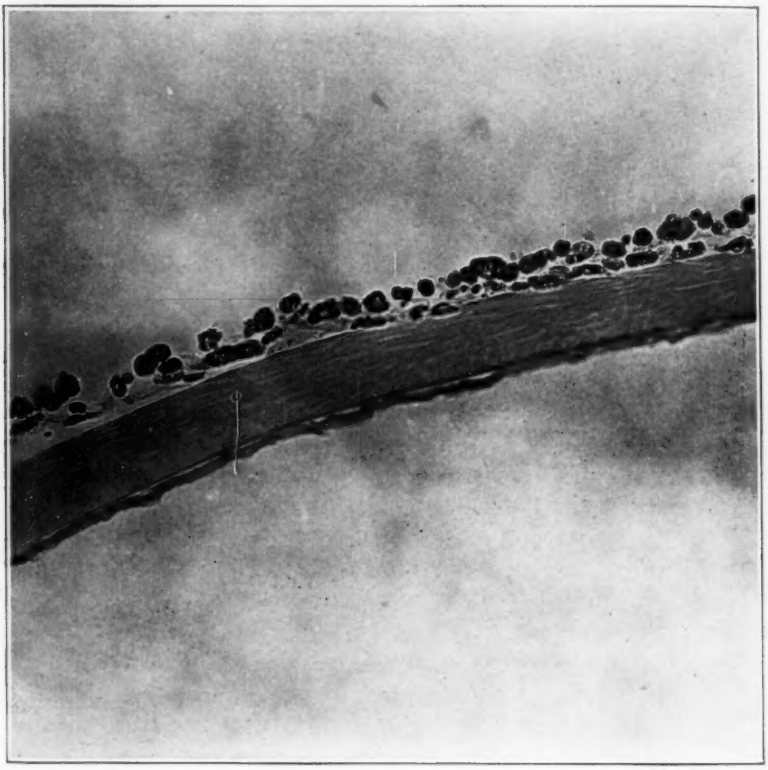

Fig. 5.—Section showing thorium dioxide–laden phagocytes on the lens capsule.

the ciliary epithelium toward the posterior surface of the lens. Another film lined the retina and turned abruptly axialward at the ora serrata. The individual fibers of the zonule were only questionably discernible until traction centrifugal to the optic axis was made on the ciliary body. This maneuver, which flattened the periphery of the lens, made the zonular fibers stand out from an apparently smooth surface. As the eye dried, the zonular fibers became distinct. The lens capsule was fixed firmly at its equator to the zonule and less firmly at Egger's line to the

vitreous. The anterior surface of the capsule was much thicker than the posterior, and when incised it gaped, permitting the lens cortex to protrude. The zonule was firmly attached to the ciliary epithelium as well as to the lens capsule, and in order to detach it from the ciliary body it was necessary to pull the epithelium from that structure. Whether or not the zonular fibers extended either posteriorly or axialward from the posterior extremity of the ciliary epithelium was undetermined, but

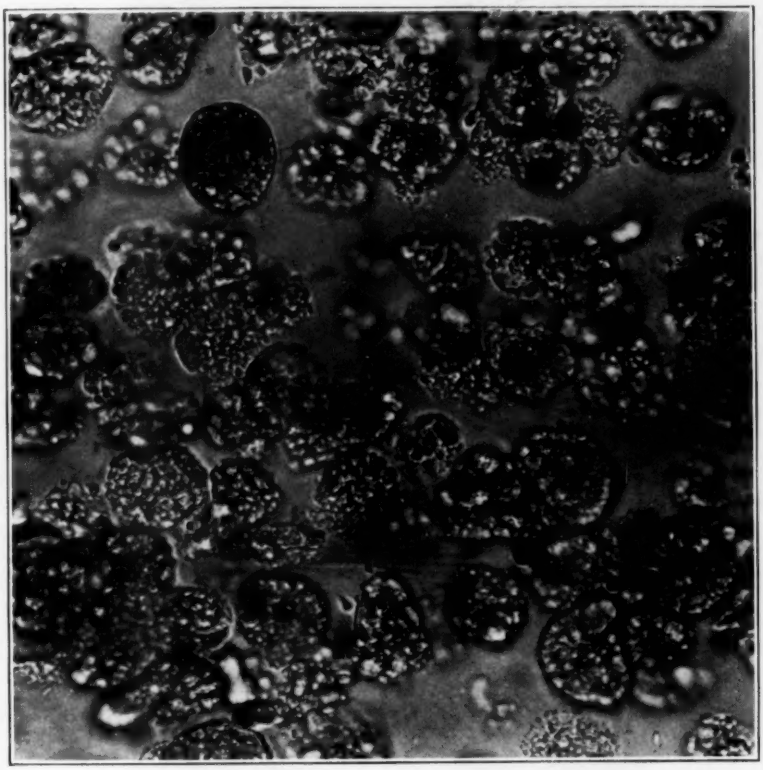

Fig. 6.—Thorium dioxide–laden phagocytes in the meshwork.

white strings of colloidal thorium dioxide were seen extending from the mother deposit of the contrast medium to the posterior extremity of the ciliary processes.

Histologic studies showed a large amount of the contrast medium as an amorphous granular mass in the vitreous, but much of it had been engulfed by phagocytes. These thorium dioxide–laden phagocytes extended from the mother deposit in thin files onto the lenticular surface and ciliary epithelium, along the zonular fibers, over the iris, into the meshwork of the filtration angle, deep into the interstices of the ciliary muscle and posteriorly over the surface of the retina. The thorium

dioxide-containing cells which lined the retina were usually on the surface, but occasionally a few cells were seen as deep as the internal nuclear layer. Near the ora serrata these phagocytes usually extended

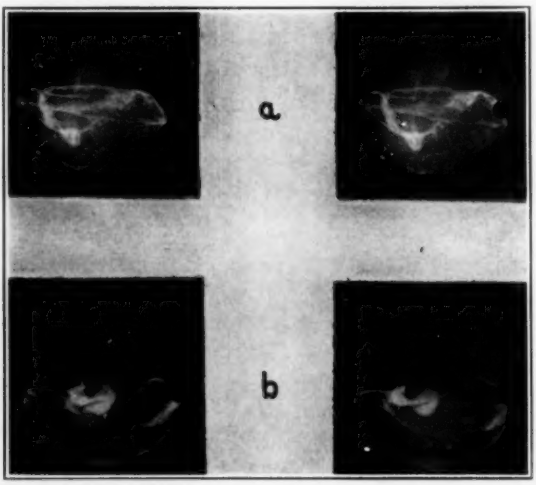

Fig. 7.—Roentgenograms showing: (*a*) the vitreous outlined by colloidal thorium dioxide in an eye under the influence of a cyclotonic; (*b*) another eye, under the influence of a cycloplegic.

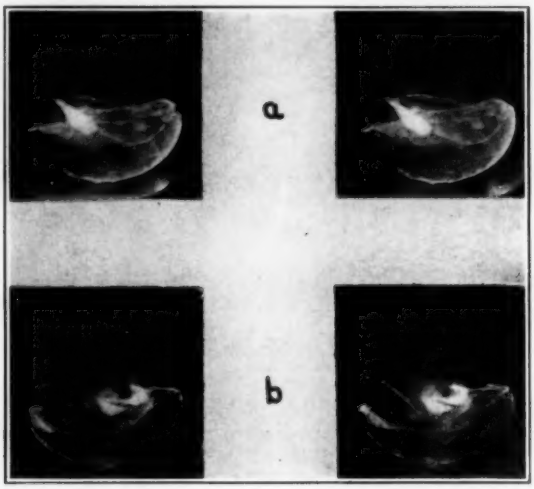

Fig. 8.—Roentgenograms showing: (*a*) the vitreous outlined in an eye under the influence of a cyclotonic; (*b*) the same eye under the influence of a cycloplegic.

into the retina as far as the pigment epithelium. Clusters of the cells were seen on the surface of the optic disk, but none were found in the optic nerve or its sheath, in the choroid or in the tapetum. They were in

greatest numbers on the ciliary epithelium but were numerous in the stroma of the iris root and the meshwork. Occasionally they were found in the vascular portion of the ciliary body, the interstices of the ciliary muscle and the channels of the limbus. It was not unusual to find small niches in the limbic tissue bordering the meshwork which contained phagocytes with thorium dioxide, and rarely a direct extension of a niche into the limbic channels was seen.

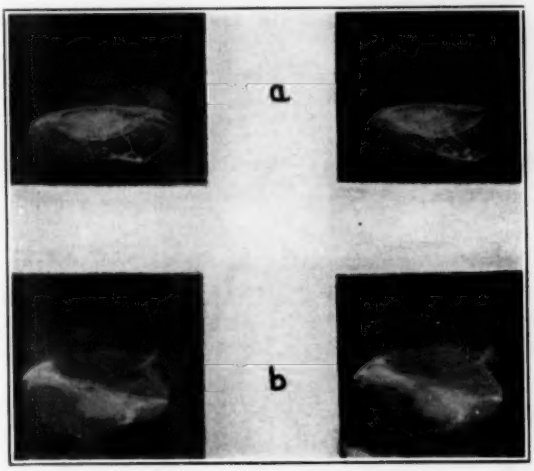

Fig. 9.—Roentgenograms showing: (*a*) the lens outlined in an eye under the influence of a cyclotonic; (*b*) the same eye under the influence of a cycloplegic.

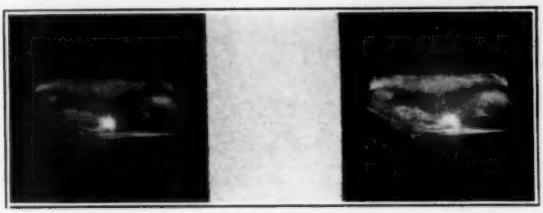

Fig. 10.—Roentgenogram showing the ciliary body outlined.

In most instances the phagocytic cell was a large round monocyte with an oval, pale-staining nucleus which contained a large nucleolus. Its cytoplasm was engorged with grayish yellow, refractile, granular material. There was much variation in the amount of thorium dioxide in the cells' cytoplasm, but in general the cells nearest the mother deposit contained the most.

Before the changes in the interior of the eye noted by means of a comparison of roentgenograms taken during miosis and mydriasis are recorded, several pertinent facts must be presented. The results were

described as a composite picture because the roentgenograms which disclosed the lens in greatest detail did not necessarily show the vitreous and other details to the best advantage. Although an attempt was made to deposit the contrast medium in a corresponding site in each eye, differences did occur. Colloidal thorium dioxide injected deep in the vitreous away from the optic axis was slow to particulate, and its distribution was poor. In contrast, thorium dioxide deposited near the posterior pole of the lens particulated and spread more rapidly.

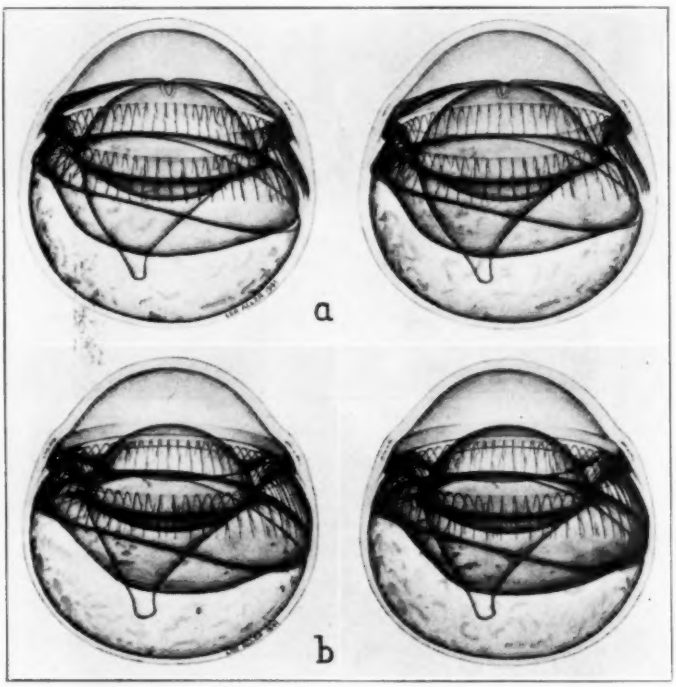

Fig. 11.—Composite stereoscopic drawings of roentgenograms of cat eyes under the influence of (*A*) cyclotonics and (*B*) cycloplegics.

The shape of the lenticular shadow on roentgenograms of an eye under the influence of a cyclotonic as compared with that of an eye under the influence of a cycloplegic showed no change in the central curvature of the anterior surface of the lens but a flattening of its periphery, an increase of central curvature and an indentation of the periphery of the posterior surface, an increase in the axial diameter but no decrease in the equatorial diameter and a slight movement of the lens toward the cornea. The anterior periphery of the tertiary vitreous in an eye under the influence of a cyclotonic was moved forward toward the lens and inward toward the optic axis. The patellar fossa had a reduced

diameter, and the posterior outline of the tertiary vitreous bulged backward and peripherally. Although the temporal portion of this division of the vitreous was larger than the nasal part, the morphologic changes of the two were similar. There was no constant change in the shape of the secondary vitreous, and, although there appeared to be a reduction in its anterior diameter, such a change could not be measured. If the choroid moved forward, as it was found to do in dogs by Hensen and Voelckers,[6] certainly it did so in cats without moving the secondary vitreous. The fine lines representing the ciliary processes made a wider angle with a plane through the posterior extremity of the ciliary body in the eyes under the influence of cycloplegics than in the eyes influenced by physostigmine. The interval between individual ciliary processes may have been narrowed slightly in the latter. The meshwork of the iris angle was well outlined in many eyes, but it was not possible to detect a constant change in its shape.

COMMENT

Colloidal thorium dioxide is claimed by its manufacturers [22] to be a highly dispersed thorium dioxide sol containing 25 per cent by volume of thorium dioxide, approximately the same amount of dextrin protective colloid and 0.15 per cent of methyl parahydroxybenzoate. It is said to be miscible under any conditions with body fluids. Observations with the loupe and the ophthalmoscope of the eyes used for this study revealed no reaction to it, and microscopic examination showed no inflammatory or degenerative changes. In a preliminary study to develop the technic, violent iridocyclitis and secondary glaucoma developed in several eyes which received more than 0.1 cc. of the contrast medium and in a few which received less but had no paracentesis and received no cycloplegic.

The intraocular distribution of colloidal thorium dioxide had definite characteristics. The hyaloid membranes, lens capsule, ciliary epithelium and zonule were coated with thorium dioxide–containing phagocytes. Why in some instances the anterior segment and in others the posterior was best outlined is a matter of speculation. However, it seemed that when the tip of the injecting needle was placed near the posterior pole of the lens the material was scattered chiefly over the surface of the secondary vitreous. Injections slightly more peripheral but at the same distance from the plane of the equator resulted in the material's being carried both forward and backward but chiefly forward. In most cases the ciliary epithelium and the vitreous were well outlined six months after injection, and after eighteen months there was no diminution of the intraocular thorium dioxide. Ophthalmoscopic studies of the eyes which received injections showed the particulation of the material to go pari passu with increased detail on the roentgenograms. Colloidal thorium dioxide injected into the anterior chamber was not carried poste-

riorly. However, in 1 eye an iridectomy was done after the injection, and the anterior segment became well outlined with the material.

Attempts to deposit colloidal thorium dioxide in the eye by injecting 15 or 20 cc. in 5 cc. weekly injections into the carotid artery or a leg vein were unsuccessful. If there are reticuloendothelial cells in the eye, they did not ingest the material as did those of the liver and spleen, which became densely radiopaque. The cats showed no ill effects from the colloidal thorium dioxide eighteen months after this procedure.

The source of the phagocytes which engulfed the material was undetermined; but if they arose from the optic nerve, as depicted by Berliner and Nonidez,[26] who injected india ink into the vitreous of rabbits, no clues to such an origin were found. A few monocytes whose nuclei were similar to those of the phagocytes and whose cytoplasm contained pigment granules but no contrast medium were found between the ciliary body and the thorium dioxide deposit. They resembled the epithelial cells of the ciliary body.

The removal of the contrast medium was slow, and the only sign of exit was the presence of phagocytes in Schlemm's canal. Perhaps the iris stroma, which often contained these cells, was an exit, but the optic nerve and its sheaths were free of the phagocytes. The significance of the material's extending from the meshwork into the interstices of the ciliary muscle is unknown.

The amount of accommodation in the cat's eye is apparently a moot point. Grossmann [7] after doing an iridectomy measured the accommodation of a cat by the retinoscope with the eye under the influence of atropine and later of physostigmine. He found 9 D. of accommodation in one meridian and 13 in the opposite. By computations Hartridge and Yamada [27] found the potential accommodation of the cat's eye to be 14 D. However, by retinoscopic examination after the use of physostigmine and atropine they demonstrated only 3.5 D. Morgan, Olmsted and Watrous [28] reported that the refraction in a cat under ether anesthesia changed from — 0.50 to + 4.00 D. on stimulation of the superior cervical ganglion. When the oculomotor nerve was cut the refraction became + 3.00, but it changed to + 10.00 on stimulation of the superior cervical ganglion. No change in the refractive power of the cat's eye was found by Barrett [29] on retinoscopic examination with the use of physostigmine and then atropine.

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26. Berliner, M., and Nonidez, J.: Transportation of Particulate Matter from the Vitreous into the Optic Nerve, Arch. Ophth. **8**:695 (Nov.) 1932.

27. Hartridge, H., and Yamada, K.: Accommodation and Other Optical Properties of the Eye of a Cat, Brit. J. Ophth. **6**:481 (Nov.) 1922.

28. Morgan, M.; Olmsted, J., and Watrous, W.: Sympathetic Action in Accommodation for Far Vision, Am. J. Physiol. **128**:588 (Feb.) 1940.

29. Barrett, J.: Accommodation in the Eyes of Mammals, Brit. J. Ophth. **22**:148 (March) 1938.

Maybe the ages of the cats used by the different investigators accounted for some of the discrepancy in the results. At any rate, the amount of accommodation represented by the changes observed in this study was unknown. The study is being continued with the use of young monkeys, which have repeatedly been shown to have considerable accommodation. The role of the sympathetic system in accommodation is also being investigated.

The zonular fibers appear to be a specialized portion of the tertiary vitreous. It is possible that they continue in an attenuated form posteriorly and axialward from their attachment to the ciliary epithelium and help form the posterior surface of the tertiary vitreous. This surface contacts the anterior border of the secondary and the periphery of the primary vitreous. If the true status of the vitreous is pictured on the films, the changes of the vitreous during accommodation are confined to the tertiary portion.

The ciliary muscle of the cat attaches anteriorly to the meshwork and the scleral spur. Posteriorly the attachment is less definite and fades out in the choroid approximately 3 mm. posterior to the ora serrata. The external surface is attached loosely to the sclera by the suprachoroidea, but internally it is fixed firmly to the ciliary epithelium. The muscle is composed of longitudinal and radial but no circular fibers, and the greatest bulk of the muscle is in a plane just posterior to the equator of the lens.

The outstanding changes in an eye under the influence of physostigmine, as shown by roentgenograms, are conoid deformation of the posterior surface of the lens, an increase of the axial diameter of the lens and an axialward forward movement of the tertiary vitreous. Since these alterations must be due to the ciliary muscle, it is assumed that the main action of the muscle is constriction of the tertiary vitreous. This sphincter-like action rolls the tertiary vitreous inward and upward against the lens and backward against the secondary vitreous. The secondary vitreous tends to expand at the ora serrata but is prevented from doing so by the attenuated posterior extremity of the ciliary muscle. The equatorial diameter of the lens does not decrease, because there are no circular fibers in the ciliary muscle to relax the anterior fibers of the zonule and the connective tissue in the anterior portion of the ciliary body blends with the meshwork fibers and tends to restrict constriction of the anterior zonule.

How the mechanism of accommodation in the cat eye corresponds to that of the eye of man is speculative. Man has circular muscle fibers near the corona of the ciliary body in addition to radial and longitudinal fibers. The diminution of the equatorial diameter of the lens, which has been described during accommodation in aniridic eyes, probably is due to these fibers. As they relax the anterior fibers of the zonule, the lens

capsule assumes a spherical shape because of an inherent tendency. Simultaneously the remaining ciliary muscle actively deforms the lens surfaces, as described in the cat. The traction of the posterior fibers of the zonule changes in direction but not in tension. That is, the zonular fibers are shifted so that their traction is directed more toward the posterior pole of the eye and less toward the equator. During maximal accommodation the lens trembles on movements of the eye because the circular muscle fibers relax the anterior zonular fibers more than the lens capsule constricts, leaving, as has been explained by Luedde,[30] the lens to be supported only by the zonular fibers attached to the posterior portion of the ciliary epithelium. In other words, both the Helmholtz and the Tscherning theory have a role in man's accommodation.

CONCLUSIONS

1. It is possible to outline on a roentgenogram many intraocular structures of an intact living eye by the technic herein described.

2. Intraocular changes produced by various drugs may be studied by this method.

3. There are three distinct divisions of the vitreous on the roentgenograms of adult cat eyes.

4. In the cat eye accommodation is brought about by compression of the posterior periphery of the lens when the tertiary vitreous is forced anteriorly and axialward by the ciliary muscle.

SUMMARY

The history of the mechanism of accommodation and its present day status are presented briefly.

A method is described whereby the interior of an intact living eye may be pictured on a roentgenogram, and the roentgenologic findings were corroborated by gross dissection and microscopic studies.

The mechanism of accommodation in the cat eye was studied and compared with the probable mechanism in the human eye.

233 A Street.

30. Luedde, W. H.: Lenticular Accommodation, Am. J. Ophth. **19**:245, 1936.

PUPILLOGRAPHIC STUDIES

I. PRESENT STATE OF PUPILLOGRAPHY; ITS METHOD AND DIAGNOSTIC SIGNIFICANCE

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AND
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Pupillography is a method of recording pupillary movements (for example spontaneous movements and reactions to light, to darkness and to near and to distant vision). It permits exact measurements of these movements and furnishes an objective clinical criterion, a graph of the reactions.

The clinical significance of pupillography has its origin in three important facts:

1. In a physiologic fact, the extreme sensitivity of pupillary movements to both physical and psychologic stimuli. As far back as seventy-five years ago, the physiologist, Schiff, called the pupil the finest esthesiometer of the body.

2. In an anatomic fact, the wideness of the area over which pupillary tracts extend within the central nervous system and outside it, both in the sympathetic and in the parasympathetic system.

3. In a pathologic fact, the peculiar vulnerability of certain parts of the pupillary pathways to both specific and nonspecific damage.

On the surface, pupillary movements appear simply as the result of an alternating change of tonus of two antagonistic muscles, the sphincter and the dilator of the iris, which are provided for by the parasympathetic third nerve and by sympathetic fibers. As simple as the play of the pupil appears, so complex is it in reality if one considers the central pathways over which it is controlled and which are only partly known.

It is known that the pupillary pathways follow the optic nerve through the chiasma opticum. That there are special pupillary fibers within the optic nerve is generally supposed but anatomically not proved. The pupillary fibers leave the visual fibers about two thirds of the way down the tractus opticus to form a proper bundle, which

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From the Department of Neurology, New York University College of Medicine.

runs to the ganglion geniculatum externum. One group of authors believe that pupillary fibers are interrupted here and that in the basal plate of the corpus geniculatum externum there arises a second neuron running toward the sphincter nucleus. Another group of authors think that no relay station exists within the corpus geniculatum externum but that the pupillary fibers go directly to the superior corpora quadrigemina, where a new relay arises, the colliculonuclear fibers, which cross to reach the Westphal-Edinger nucleus. According to Behr the maculopupillary fibers are in connection with both the ipsilateral and the contralateral nucleus. According to Foerster, Gagel and Mahony the sphincter nucleus does not lie in the Westphal-Edinger bilateral nucleus but in the unique central-medial nucleus ventral to the Westphal-Edinger nucleus. According to Ranson there is no relay in the superior corpora quadrigemina but cephalad in the pretectum. From the sphincter nucleus the efferent pathways of the light reflex go through the ciliary ganglion.

The localization of the pupillary center for reaction to near and to distant vision is not known. It must, however, be above the sphincter center bilaterally and is in direct and crossed connection with the two sphincter centers. The visual impulses to these centers are believed to pass to the occipital cortex and to be relayed to the frontal lobes and then once more relayed to reach (through the internal capsule, the pes pedunculi and the mesial fillet) the third nerve nucleus of the opposite side.

The dilator pupillae is provided for by sympathetic fibers, which, unlike the parasympathetic fibers for the sphincter, are not interrupted in the ciliary ganglion. They come from the superior cervical ganglion and run with the internal carotid nerve and the carotid plexus, entering the skull with the internal carotid artery; they are in connection with the gasserian ganglion and enter the orbit with the first branch of the fifth nerve. It is not known whether all sympathetic dilator fibers run through the ciliary ganglion or whether part of them accompany the vessels to the iris. The sympathetic pathway from the upper cervical ganglion to the iris (third neuron) is subordinated to the second neuron, with its center (ciliospinal center) in the eighth cervical, first dorsal and second dorsal segments of the cord; it is similarly subordinated to the first, or diencephalic, neuron, the pathways of which descend from the hypothalamus through the tegmentum of the midbrain to the anterior-lateral funiculi of the cord. The exact localization of the nuclei from which the diencephalic pupillary pathways rise is not known.

The largeness of the area which the pupillary pathways traverse, and the fact that they are in connection with many upper and lower

parts of the brain, led Behr to declare that there is hardly any nervous function without a direct or indirect influence on the reactions of the pupil. Any one familiar with the literature knows that pupillary disturbances have been described in association with nearly every illness—not only illnesses of nervous or mental origin but internal maladies and even general infections.

METHOD

Pupillography is a method of recording pupillary movements; it permits the exact measurement of these movements.

We shall say only a few words about the method and refer the reader for all details to former publications.[1]

Figure 1 shows the most recent type of equipment as built in the neurologic department of New York University College of Medicine.

The foundation of pupillography is cinematographic equipment which is enclosed in sound-proof box *A* (fig. 1) and which is driven by a motor situated in sound-proof box *B*. The patient sits in the chair, *C*, with his head against the head rest, *D*, and his chin at the chin rest, *E*. His eyes are directly opposite the lens, *F*, of the camera, which simultaneously records the movements of the two pupils. It is well to emphasize that the movements of the two pupils are recorded simultaneously on the same film; exact measurements of direct and consensual reactions which are a functional unity are thus permitted. Their reciprocal modifications are of great diagnostic value.

Light stimulation of the right or the left pupil is mechanically produced at timed intervals with a synchronous motor interrupter, *G*. The motor operates a shutter which can be opened for 1, ½, ⅕, 1/10, 1/25 and 1/50 of a second at regular intervals of 1, 2, 3, 5 or more seconds.

1. Löwenstein, O.: Experimentelle Beiträge zur Lehre von den katatonischen Pupillenveränderungen, Monatschr. f. Psychiat. u. Neurol. **47**:194, 1920; Ueber eine Methode zur kinematographischen Darstellung der Pupillenphänomene und den Ablauf einiger Pupillenreflexe, Zentralbl. f. d. ges. Neurol. u. Psychiat. **45**:300, 1926; Ueber den Ablauf einiger Pupillenreflexe: II. Mitteilung, ibid. **45**:612, 1926. Löwenstein, O., and Westphal, A.: Kinematographische Untersuchungen über Störungen der Pupillenbewegungen mit besonderem Hinblick auf den sogenannten Spasmus mobilis, Arch. f. Psychiat. **82**:315, 1927. Löwenstein, O.: Ueber die Variationsbreite des Lichtreflexes und der Psychoreflexe der Pupillen: Beiträge zur Kenntnis der psychophysischen Konstitution, ibid. **82**:285, 1927; Ueber die sogenannte paradoxe Lichtreaktion der Pupille: Klinische und experimentell-kinematographische Untersuchungen über ihre Symptomatologie und ihr Wesen, Monatschr. f. Psychiat. u. Neurol. **66**:148, 1927; Ueber die Natur der sogenannten Pupillenunruhe: Experimentell-kinematographische Untersuchungen, ibid. **66**:126, 1927.

The beam of light thrown into the right or the left eye has a sharply limited circular cross section and is covered medially by a screen; thus it cannot be seen by the left eye when it is cast into the right eye, and vice versa. Its intensity can be varied and its duration—like that of

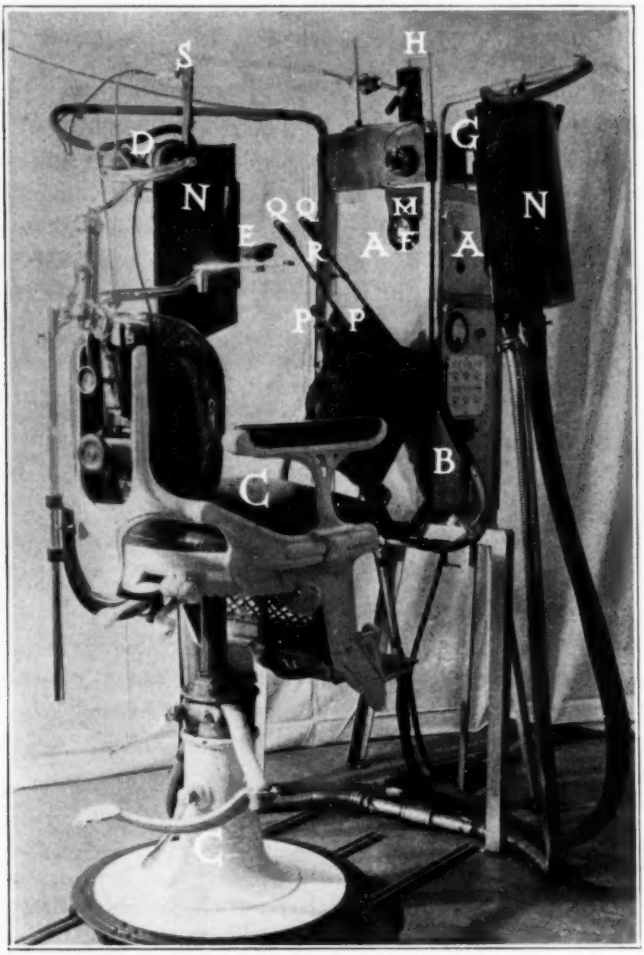

Fig. 1.—Pupillographic equipment.

all other sensory or psychic stimuli—can be recorded on the drum, *H*, which rotates synchronously with the motor-driven interrupter, *G*. A time recorder (1/5 second) writes its marks simultaneously by means of an electromagnet and a light sign on the drum and on the film.

In order to prevent convergence disturbances, the subject's vision is focused on infinity by means of a small nonstimulating light point reflected by a mirror, *M*.

The chair, *C*, runs on rails so that the subject can be brought as close to or withdrawn as far from the lens of the camera as necessary.

Our greatest technical problem for years has been to photograph the pupil and at the same time maintain nonstimulating light conditions; the light intensity must be sufficient to facilitate cinematography and at the same time not sufficient to stimulate the pupils to contraction. In order to surmount the vicious circle involved, we used blue-violet glasses as light filters in front of the surfaces of the illumination bodies *(N, N)*, which were placed close to both sides of the head and as tangentially as possible to the eyes. This arrangement caused the pupil to remain dilated in spite of an effective, relatively powerful illumination, which permitted the pupillary movements to be photographed.

Since 1937 we have employed infra-red filters, which permit us to perform pupillography under the conditions of—practical—darkness. We installed two small infra-red reflectors *(P, P)* in front of and below the patient but kept the lateral lamps *(N, N)* for excited patients, for restless children and, particularly, for animal experiments. The light filters are interchangeable; so the infra-red filters can be replaced by filters of another color, as is sometimes necessary for more rapid production of the pathologic phenomena of asymmetric fatigue (Wedensky effect).

In order to elicit the reflex to darkness, tests must be made under conditions in which the light is constant and darkness is the periodic stimulus. Two small lamps *(Q, Q)*, separated from each other by a screen (so that the right eye cannot see the left lamp, and vice versa), burn continuously for a period of twelve minutes, which is the time necessary for adaptation. The light of one or the other of these lamps is periodically interrupted by the motor interrupter, *G*.

When the reaction to near and to distant vision is to be examined, the subject focuses his eyes alternately on the movable near point, *R*, and the distant point in the mirror, *M*.

In front of the patient, on a small board, a certain number of small nonluminous infra-red lamps are fixed. These operate individually with the light stimuli, the sensory stimuli, the darkness stimuli, the near point, the far point and so on, thus constituting in the film itself a direct time control system.

In figure 2 we show a typical film. Each picture is measured, and the results of the measurements are translated to a graph in order to give a continuous curve of the magnitude of the diameter of the pupil as the ordinate against time as the abscissa.

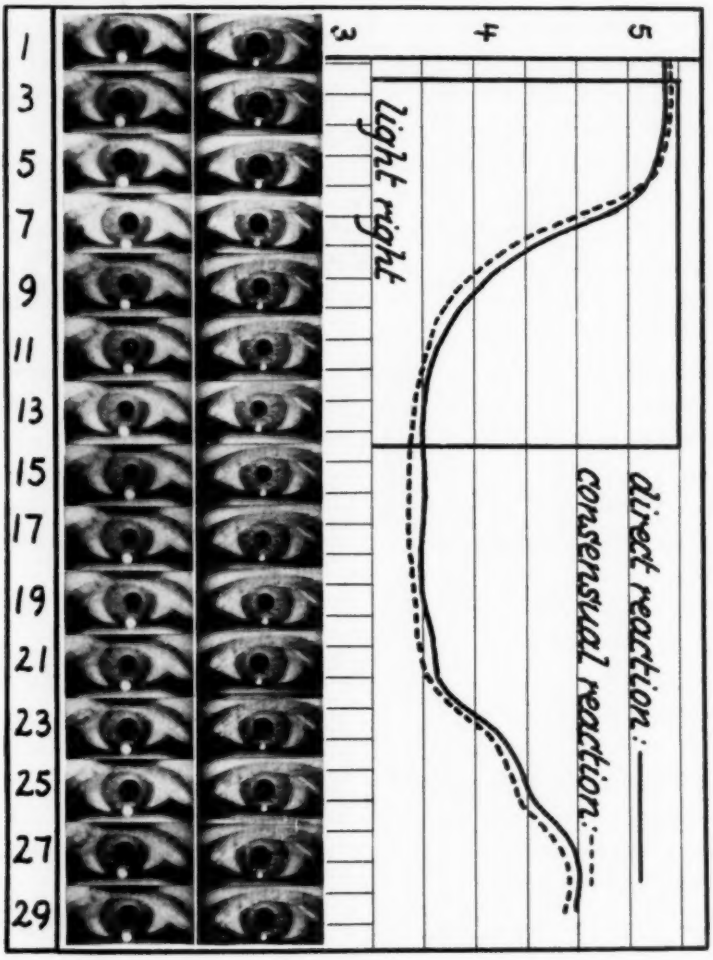

Fig. 2.—Typical film. The patient was a Negro with a very dark iris. Each second picture was omitted. Picture 1 shows the eyes in darkness; pictures 3 to 13, the eyes with the light stimulus applied to the right eye, with contraction of both pupils, and pictures 14 to 29, the eyes in darkness, with dilation of both pupils.

THE REFLEX TO LIGHT

The normal reflex to light consists of a contraction of both pupils and redilation. The contraction begins after a latency period of about

0.2 to 0.28 second but increases significantly above this figure under conditions of fatigue or under other physiologic conditions. The duration of the contraction amounts to about 0.45 second or more. The course of the reflex itself is relatively independent of the time of stimulation; a full reflex contraction is obtained by stimulation periods of $\frac{1}{50}$ second or less. The contraction begins with a rapid movement, which slows down after 0.2 to 0.3 second.

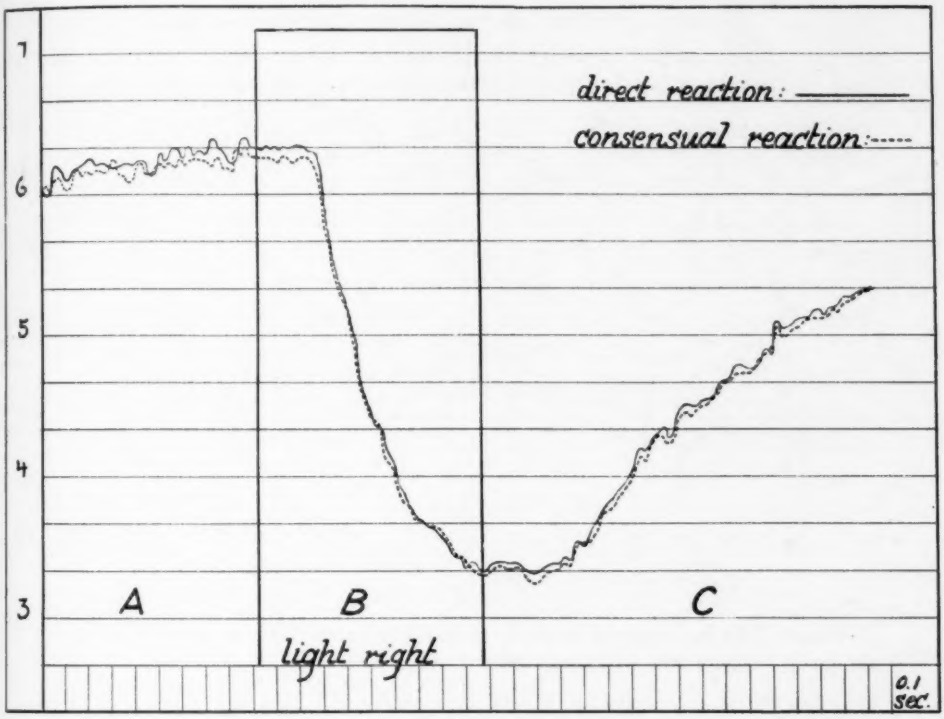

Fig. 3.—The normal reflex to light (fifty pictures per second). *A*, first phase (darkness), pupillary unrest; *B*, second phase (light stimulation), 0.28 second latency period preceding the contraction phase; *C*, third phase (darkness), dilation phase.

When the stimulation time takes 1 second, the contraction frequently continues for a period of 0.2 to 0.3 second after the light stimulus has ceased.

The redilation begins after a latency period which is equal to or longer than the latency period for contraction. The redilation, too, is rapid in its first part and slower in its last part.

When the pupils are normal, the direct and the consensual reaction to light are fully identical, as shown in figure 3.

We find in the normal subject four different types (fig. 4) of reaction to light. The first type is characterized by a rapid contraction and a rapid dilation; the second and most common type, by a prompt contraction and a sluggish dilation; the third type, by a sluggish contraction and a prompt dilation, and the fourth type, by a sluggish contraction and a sluggish dilation.

These four types represent four different forms of equilibrium between sympathetic and parasympathetic innervation. They are constitutionally conditioned and are identical in monozygotic twins but may be different, according to the biologic probability, in bizygotic twins. They make it possible to distinguish between both sympathetic and parasympathetic hypotonia and hypertonia. It was found that a

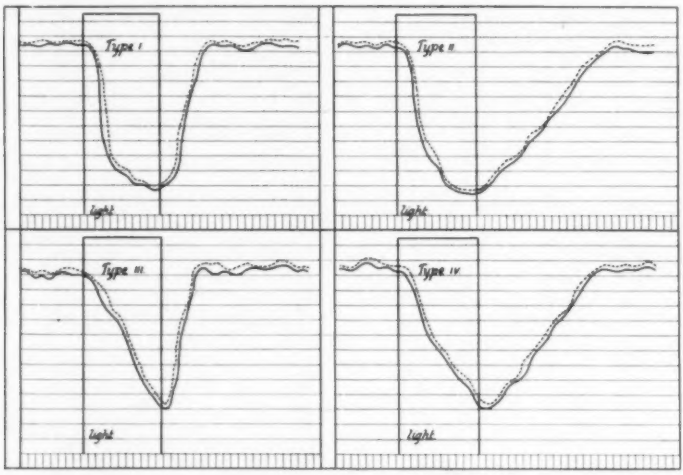

Fig. 4.—The four types of pupillary reactions to light. The unbroken lines show the direct reaction and the broken lines the consensual reaction.

relationship exists between the fourth type and schizophrenia and between the first type and manic-depressive psychosis.

THE PHENOMENA OF FATIGUE

Up to now it was generally supposed that light reflexes, like other vegetative reflexes, show no fatigue. This seemed to be a *conditio sine qua non* for the maintenance of life. The physiologic problem was therefore: How is it possible that these reflexes never tire?

Pupillographic researches show that the pupillary reflexes do tire; they even tire rather quickly. If we repeat the light stimulation several times by means of our mechanically operated interrupter (for instance, in stimulation periods of 1 second and intervals of 3 seconds) the

phenomena of fatigue may be seen very soon. These phenomena occur in about seven distinct stages (fig. 5) and end in absolute rigidity, or complete exhaustion of the reflex. The first sign of fatigue is a diminishing extent of the reaction. The second stage is a prolongation of the physiologic latency period, which soon goes to more than 0.3 second and gradually increases to more than 0.4 second. In the third stage, an initial dilation precedes the reaction to light, during which the amplitude of contraction diminishes. In the fourth stage, the initial dilation is replaced by a second prolongation of the physiologic latency period both for contraction and for dilation. The fifth stage shows a decrease of the dilation. In the sixth stage, there is a second phase of initial dilation, which is no longer followed by contraction. In this stage, the reaction resembles the so-called paradoxic reaction to light, hitherto considered to occur exclusively in cases of dementia paralytica or tabes dorsalis but now proved to occur physiologically as a transient stage of normal fatigue. The seventh stage is a stage of immobility.

Much work was done in an attempt to decide the question of whether we were dealing with real pupillary fatigue or possibly with another phenomenon (e. g. adaptation). For the details concerning this work, we refer the reader to the original literature.[1a]

The argument as to whether or not fatigue phenomena are localized in the retina can be answered, since we found that after we obtained a certain degree of fatigue by stimulating one eye (while the other eye was kept in full darkness) the nonstimulated pupil was in the same stage of fatigue. This could be demonstrated by the sudden application of a light stimulus to the hitherto nonstimulated eye, in which now either no reaction or a reaction of fatigue was elicited.

The course of fatigue runs through seven well developed stages, and this "law of fatigue" governs the fatigue process of the pupil. It is possible that in cases of increased fatigability the different stages follow one another more quickly than in other cases. It is also possible that one or another stage may be shorter or less well pronounced in one case than in another. We could never find a case, however, in which the "law of fatigue" was not followed.

This law governing normal fatigue is of great importance to pathology, for in cases of disintegrating function (in neurosyphilis, for instance) the reaction types of the seven stages, which are transitory in cases of physiologic fatigue, exist as more or less permanent and fixed types of reaction in the first response to light (without preceding fatigue).

1a. Löwenstein, O.: Der psychische Restitutionseffect: das Prinzip der psychisch bedingten Wiederherstellung der ermüdeten, der erschöpften und der erkrankten Funktion, Basel, Benno Schwabe & Co., 1937.

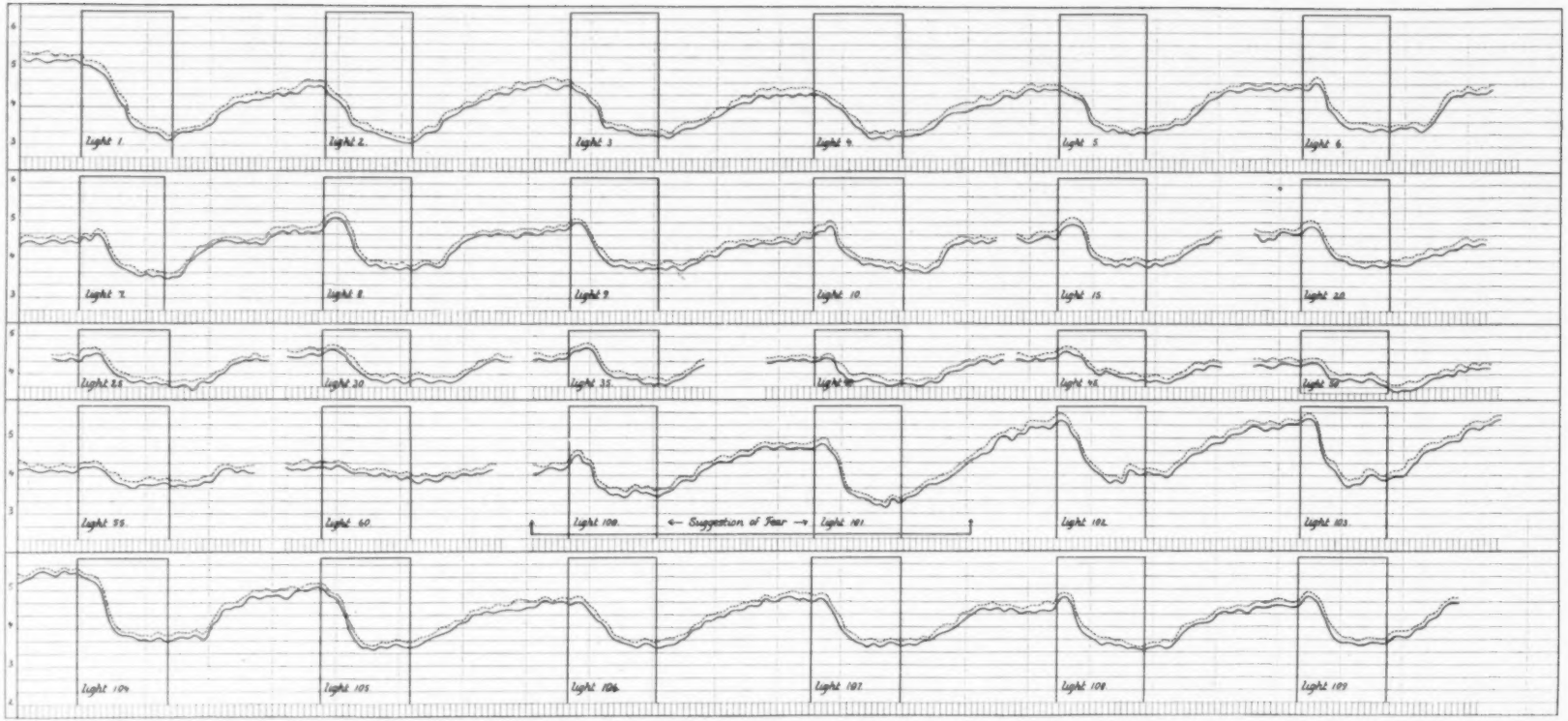

Fig. 5.—Fatigue phenomena and the psychosensory restitution phenomenon.

This "law of analogy between physiologic fatigue and pathologically disintegrating function" [1] will later on be considered further. It makes possible the recognition of disease, neurosyphilis for instance, in early stages of disintegration.

THE PSYCHOSENSORY RESTITUTION PHENOMENON

We have seen the pupillary reactions fatigue to a point where the pupils no longer respond (fig. 5, light stimulation number 60). Beginning with about the sixtieth light stimulation the pupils were immobile to light. Nevertheless we continued to stimulate the pupil up to the one hundred and tenth time. After the ninety-ninth stimulus a suggestion of fear was introduced by threatening pain; we saw that to the degree to which this suggestion was accepted the pupillary reaction was gradually restored. The one hundredth stimulus met with a pupil which was not yet dilated; in other words, it had kept the size which it had before, when it was immobile. Nevertheless it contracted approximately in the same form in which it contracted at about the twentieth stimulation. We saw the pupil pass gradually, step by step, backward through all the stages of fatigue through which it had passed before being exhausted. Six light reactions after the suggestion of fear had begun, the pupil (increasing in size) reached its highest degree of restoration; then it gradually fatigued again. It must be emphasized that all the factors which made the pupil small and inactive continued but were made ineffective by the intercalated psychologic suggestion.

It is possible to replace the fear suggestion induced in the experiment of figure 5 by some other psychologic suggestion, e. g. a suggestion of joy or other emotion. It is also possible to use a purely sensory stimulus, such as a noise stimulus or the prick of a pin. The result is the same in each case except that a sudden and strong sensory stimulus, for instance a sound stimulus, produces not a gradual but a sudden restoration (not step by step over a certain number of stages). But, as is shown in figure 5 and as has frequently been seen in pathologic conditions, the restoration effect is independent of the dilatation reflex of the pupil, frequently preceding the restoration; it sometimes, in pathologic conditions, even exists when the dilatation no longer exists.

This interesting phenomenon is called the "psychosensory restitution phenomenon." [1a] It represents a real restoration of the exhausted function, probably by means of the liberation of epinephrine. It is a sympathetic brain reflex.

THE REFLEX TO DARKNESS

If under the conditions described, in which the light is constant, one pupil is acted on by a darkness stimulus for the duration of about 1 second, a reflex to darkness is elicited both directly and indirectly.

The pupil dilates and the dilation period is followed by a "secondary" contraction and a redilation (fig. 6, first line). This reflex also shows a latency period, which, so far as is known now, is longer than the latency period preceding the light reflex. The reflex to darkness also can be fatigued, and the process of fatigue is characterized by a prolongation of the latency period, which after some time is replaced by an initial

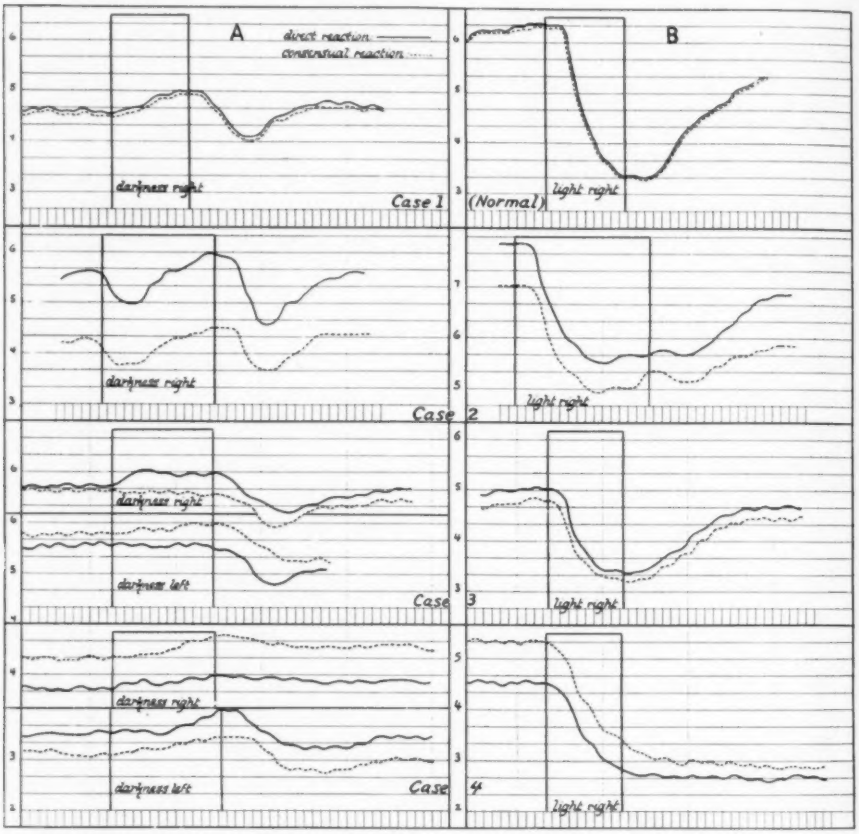

Fig. 6.—*A*, reflex to darkness, and *B*, reflex to light in the same patient.

contraction preceding dilation. The details of the tiring stages are not yet well known. It is known, however, that, as in the light reflex, the direct and the indirect reactions are always identical.

The reflex to darkness appears to be an independent reflex. It is particularly independent of the reflex to light (fig. 6 *B*). We observed pathologic conditions in which the reflex to darkness was intact but the reflex to light was absent, and vice versa. We also observed pathologic conditions in which the primary dilation within the reflex to darkness

was absent but the secondary contraction and redilation were present (fig. 6, case 3, second line) or in which the secondary contraction and redilation were absent but the primary dilation was present (fig. 6, case 4, first line).

It appears probable according to clinical observations that the pathways for the reaction to darkness are different from those for the reaction to light, that they run with the visual pathways to the occipital lobe and thence to the hypothalamus. On the other hand, it is known that there are direct connections between the retina and the nucleus supraopticus and other parts of the diencephalon which possibly are pathways for the reaction to darkness. Present knowledge as to this point is incomplete. The reflex to darkness is—primarily—a sympathetic reflex, whereas the reflex to light is—primarily—a parasympathetic reflex.

THE REFLEX TO NEAR AND TO DISTANT VISION

The reflex to near vision consists of a contraction and that to distant vision of a dilation of the pupil. In normal eyes the movements of the two pupils are identical. The contraction to near vision is about as extensive as the contraction to light (fig. 7, first line, and fig. 15, third line), but it is generally acknowledged (not proved) that the force of the reaction to near vision is stronger than that of the reaction to light. Up to the present the general opinion has been that the movements of the pupils in reaction to near vision are only synkinesias with the convergence movements of the eyes, but there are urgent reasons for the opinion that they are independent reflexes (Löwenstein [2]).

Anisocoria due to a peripheral sympathetic lesion does not influence the reaction to near vision (fig. 7, second line), but there may exist in other conditions different degrees of diminution of this reflex, bilaterally or unilaterally. The unilateral diminution results in anisocoria which exists only during the contraction period and particularly at the height of contraction. We call this anisocoria dynamic anisocoria (fig. 7, *B-II*), as opposed to that type which (fig. 7, *B-I*) exists before the contraction begins and which persists or even diminishes during the contraction, which we call static anisocoria.

In figure 7 (*B-III*, *B-IV*, *B-V* and *B-VI*) are shown different degrees of contraction varying from a decreased reflex to near vision to complete absence of this reflex. These anomalies may be either equal on the two sides or unequal, as in *B-V* of figure 7, where even a tendency toward an initial paradoxic dilation is found. *B-VII* of figure 7 shows a unilateral pupillotonic reaction.

2. Löwenstein, O.: (*a*) Les troubles du réflexe pupillaire à la lumiere dans les affections syphilitiques du système nerveux central: Contribution pupillographique au diagnostic précoce de la syphilis du système nerveux central (lues nervosa), Paris, Gaston & Cie, 1939; (*b*) Pupillography: Its Significance in Clinical Neurology, Arch. Neurol. & Psychiat. **44**:227 (Aug.) 1940.

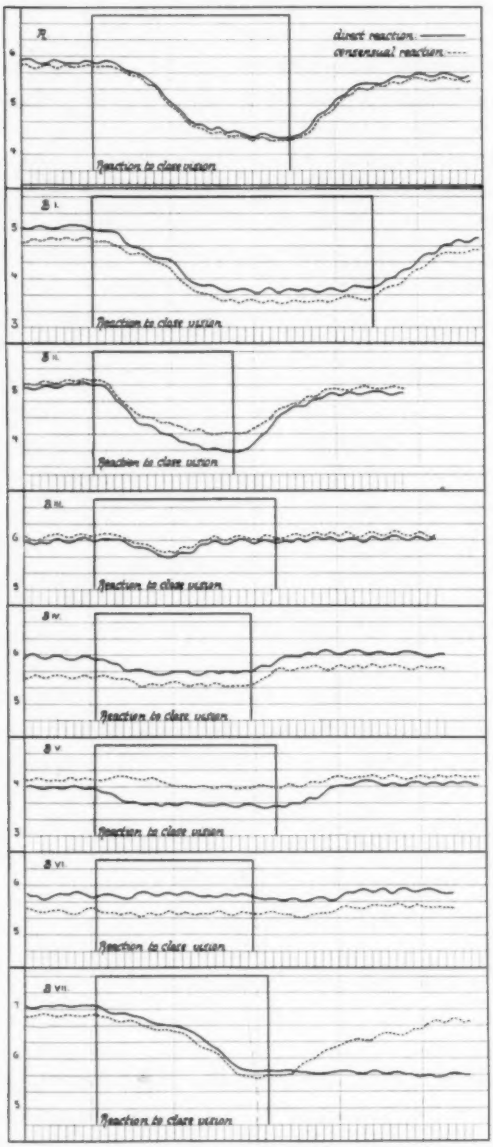

Fig. 7.—Reactions to near and to distant vision. *A*, normal, and *B-I* to *B-VII*, in pathologic conditions. *B-I*, static anisocoria, normal reaction; *B-II*, dynamic anisocoria; *B-III*, decreased reflex, *B-IV*, decreased reflex with static anisocoria; *B-V*, both the direct and the consensual reflex diminished, dynamic anisocoria; *B-VI*, anisocoria, absence of the reflex; *B-VII*, unilateral pupillotonic reaction.

THE WESTPHAL-PILTZ (ORBICULARIS) PHENOMENON

The Westphal-Piltz phenomenon, also generally considered a synkinesia, is a regular reflex consisting of a contraction of both pupils on an attempt to shut one or both eyes while the lids are mechanically held open. The consensual and the direct reaction are identical. Figure 8 shows the pupillographic feature of this phenomenon. The first line represents the reaction on an attempt to close both eyes and the second and the third line the reaction on an attempt to close, respectively, the right or the left eye.

As yet the Westphal-Piltz phenomenon has no particular diagnostic importance, nor has it been the object of more extended pupillographic

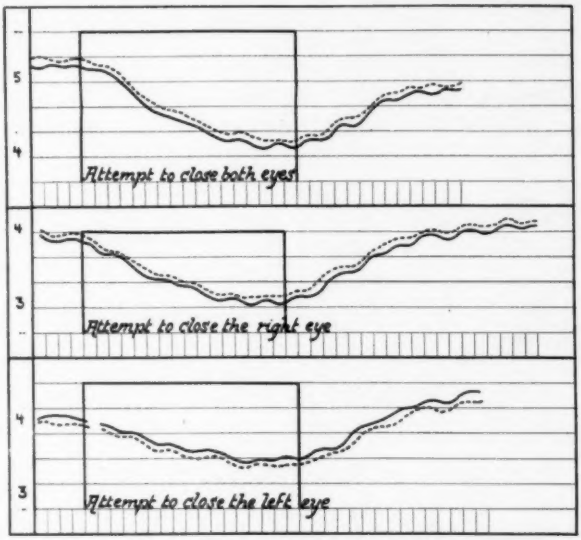

Fig. 8.—Orbicularis phenomenon (Westphal-Piltz).

researches. We found it sometimes present in cases in which the light reflex was absent, either in Argyll Robertson pupils or in absolutely immobile pupils, but we found it absent in cases, for example, of Adie's syndrome, in which it was present in the unaffected pupil. We found it in association also with other central sympathetic lesions.

THE TONOHAPTIC REACTION

We have already emphasized the relationship between catatonia and the schizoid constitution, on the one hand, and the fourth type of light reflex, on the other hand. In 1933 we [3] found that the fourth type of

3. Löwenstein, O., and Westphal, A.: Experimentelle und klinische Studien zur Physiologie und Pathologie der Pupillenbewegungen, mit besonderer Berücksichtigung der Schizophrenie, Berlin, S. Karger, 1933.

reaction to light is seen especially often in introverted persons belonging to the schizophrenic group. In such persons, by an exaggeration of its characteristics, this type transforms itself into a fifth type, with a relatively long latency period, marked sluggishness, a mild contraction and an equally sluggish redilation. In cases of catatonia another type of reaction to light was observed,[3] characterized by a long latency period, a rapid reaction to light and a long latency period for the redilation, followed by a good dilation.

A special type of permanently heightened tonus causes these reactions, which we call tonohaptic reactions. We found them in association with postencephalitic lesions both with and without the parkinsonian syndrome. Later on we found them in cases of diabetes insipidus, dystrophia adiposogenitalis, Simmond's cachexia, Wernicke's crampus neurosis and retinitis pigmentosa (Franceschetti). We found a relation between tonohaptic reactions and lesions either in the diencephalon or in its connections with the mesencephalon (Westphal; Lowenstein; Franceschetti). Many patients with so-called psychopathy, which had been considered constitutional, hereditary or even psychogenic, showed tonohaptic responses.[4] They were frequently suffering from obsessions and phobias which were in the center of the psychopathic syndrome, and many had a history of encephalitis in early or late childhood.

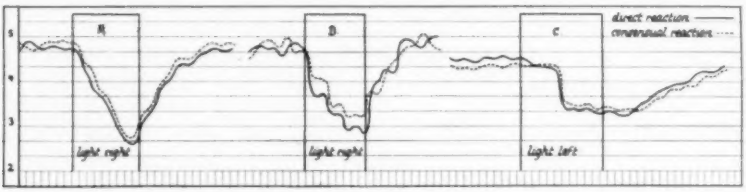

Fig. 9.—*A*, normal reaction to light; *B*, reaction to light by steps (psychogenic); *C*, tonohaptic reaction.

THE REACTION TO LIGHT "BY STEPS" (IN COGWHEEL FASHION)

A type of reaction to light exists in which contraction does not happen in a single sweep but contraction or, more frequently, redilation occurs by steps (in cogwheel fashion), as shown in figure 9. We observed this type of reaction in cases of so-called hysteria with somatic symptoms. It is constitutional, as we saw it several times both present

4. Löwenstein, O.: Pupillographie et psychopathie constitutionnelle, Congrès des Médecins aliénistes et neurologistes, Neuchâtel, Switzerland, July 20-25, 1936; Les psychopathies soi-disant constitutionnelles de l'enfance à la lumière de la pupillographie, Bull. de neuro-psychopath. infant., November 1938.

and uniform in identical twins. It corresponds to the phenomena of inhibition and excitation of striated muscle tonus described as secondary reactions after sensory stimulation.[5]

THE ANALOGY BETWEEN PHYSIOLOGIC FATIGUE PHENOMENA AND PATHOLOGIC DISINTEGRATION PHENOMENA

We [6] have already emphasized that the law governing normal fatigue is of great importance for pathology. In cases of degenerating function, of neurosyphilis for instance, one finds after the first stimulation types of reaction to light which are identical with the reaction types in more or less advanced stages of physiologic fatigue. It is not necessary to emphasize that this identity is of phenomenologic exclusively and not of genetic nature. It is evident that the complete Argyll Robertson phenomenon, i. e. absence of a reflex to light with presence of a reflex to near and to distant vision, does not develop from one day to the next. A long evolution is necessary, and this evolution generally has a certain number of stages which phenomenologically are identical with the transient stages of physiologic fatigue.

These pathologic reactions (as expressions of a permanent injury and not as results of a preceding fatigue) can be detected as early symptoms of organic lesions within the pupillary pathways, for example in cases of syphilitic lesions of the central nervous system in their beginning and frequently long before other symptoms appear.

The degeneration types which are detected in this way are generally not symmetric on the two sides. It is possible that the right pupil will show the second stage of fatigue while the left pupil shows the first, the fourth or any other stage or even a normal reaction.

Figure 10 is the pupillogram of a woman whose 10 year old son, considered an imbecile, was found on examination at the hospital to have a number of symptoms of congenital syphilis. The mother did not show any symptom of syphilis, neurologic, serologic or dermatologic. She did not know anything about a syphilitic infection, which must have been asymptomatic. Her pupils showed a reaction to light corresponding to the third stage of fatigue on the left side and the fifth stage on the right side. She refused to be treated, and one year later she had dementia paralytica, the pupillographically detected syndrome having been the only early, preclinical sign.

5. Löwenstein, O.: Experimentelle Hysterielehre; zugleich ein Versuch zur experimentellen Grundlegung der Begutachtung psychogener Unfallfolgen, Bonn, Friedrich Cohen, 1923.

6. Löwenstein, O.: Die Störungen des Lichtreflexes der Pupille bei den luetischen Erkrankungen des Zentralnervensystems: Beiträge zur Frühdiagnostik der Lues nervosa, Basel, Benno Schwabe & Co., 1935. Löwenstein, O., and Guillerey, M.: Diagnostic précoce de la syphilis cérébrale par la méthode pupillographique, Congrès des médecins aliénistes et neurologistes, Neuchâtel, Switzerland, July 20-25, 1936. Löwenstein.[2a]

Figure 11 is the pupillogram of a man about 50 years of age who had always had nervous symptoms ("neurasthenia"), at the center of which were more or less typical reactive depressions. He came to the

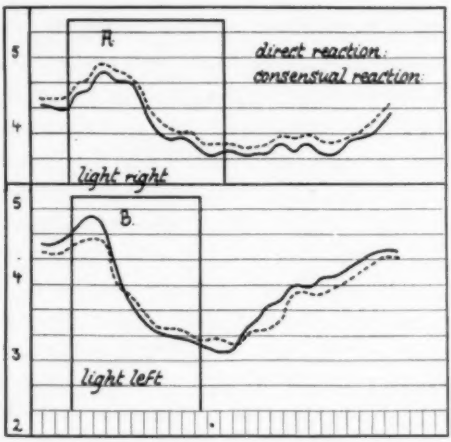

Fig. 10.—Pupillogram of a woman in the preclinical stage of dementia paralytica, one year before the first clinical signs appeared. The reflexes to light show pathologic types.

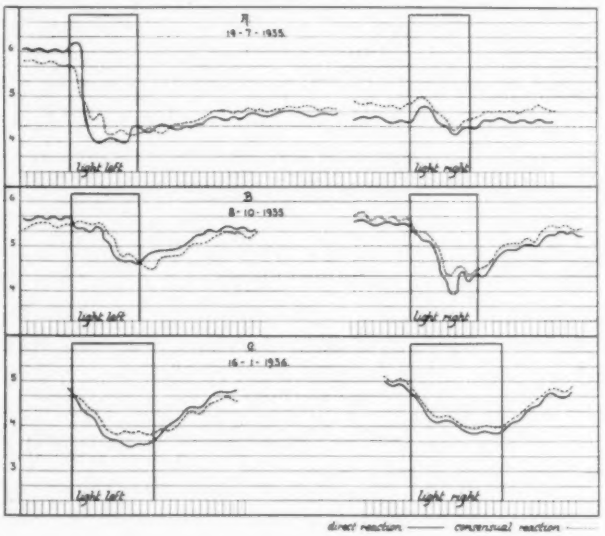

Fig. 11.—Pupillary reactions to light in the preliminary stage of dementia paralytica. *A*, before treatment; *B*, three months after treatment was begun; *C*, three months later.

hospital in 1935 after having been ill for nearly three years with indefinite nervous symptoms. No organic symptoms had been detected, but for

months he had been neglectful of his person and disinterested in his work and in his family. A pupillographic examination disclosed an organic syndrome. Figure 11 *A* discloses on the left side a good contraction, but only after an initial dilation, a reaction corresponding approximately to that of the first stage of fatigue. On the right side is the reaction of the fifth stage of fatigue. After 4 Gm. of arsphenamine, the Wassermann reaction of the cerebrospinal fluid, hitherto always negative, became positive; the number of lymphocytes rose from 5 to 18, and the test for globulin became positive. After 8 Gm. of arsphenamine these tests were negative again. Three months later we obtained the pupillogram reproduced in figure 11 *B*, and after another three months that of 11 *C*. The patient improved greatly, was treated with fever therapy and has been in good health for more than five years. The diagnosis was the preliminary stage of dementia paralytica.

ASYMMETRIC FATIGUE SYMPTOMS

Sometimes the symptoms of organically conditioned asymmetry in the pupillary reactions are still more obscure and not at all manifest in the first reaction. We have to fatigue both pupils (one after the other and in two different series of experiments) by stimuli of the same rhythm in order to find out whether or not the same stages of fatigue occur after the same number of stimulations for the right and for the left side.

Figure 12 represents an example. It discloses on the left side an initial dilation (third stage of fatigue) following the second light stimulation, whereas the right side does not show fatigue symptoms at all. The patient was a man 25 years of age who had contracted a syphilitic infection five years previously; he had been well treated and tests of his blood and cerebrospinal fluid were negative. When he was seen two months later, his pupillographic examination showed an initial dilation, that is to say an originally conditioned fatigue symptom, in the first reaction of the left pupil and in the third reaction of the right pupil; an active syphilitic process of the central nervous system was postulated and was proved by the positive result of an antisyphilitic treatment.

THE PSYCHOSENSORY RESTITUTION PHENOMENON IN ASSOCIATION WITH ORGANIC LESIONS

Figure 12 discloses that the sound stimulus applied between the fourth and the fifth light stimulus enlarged the left pupil and abolished the initial dilation. It reveals that even the restored fifth reaction to light was not as prompt as the corresponding reaction of the right pupil and that the prolongation of the latency period seen in the first reaction

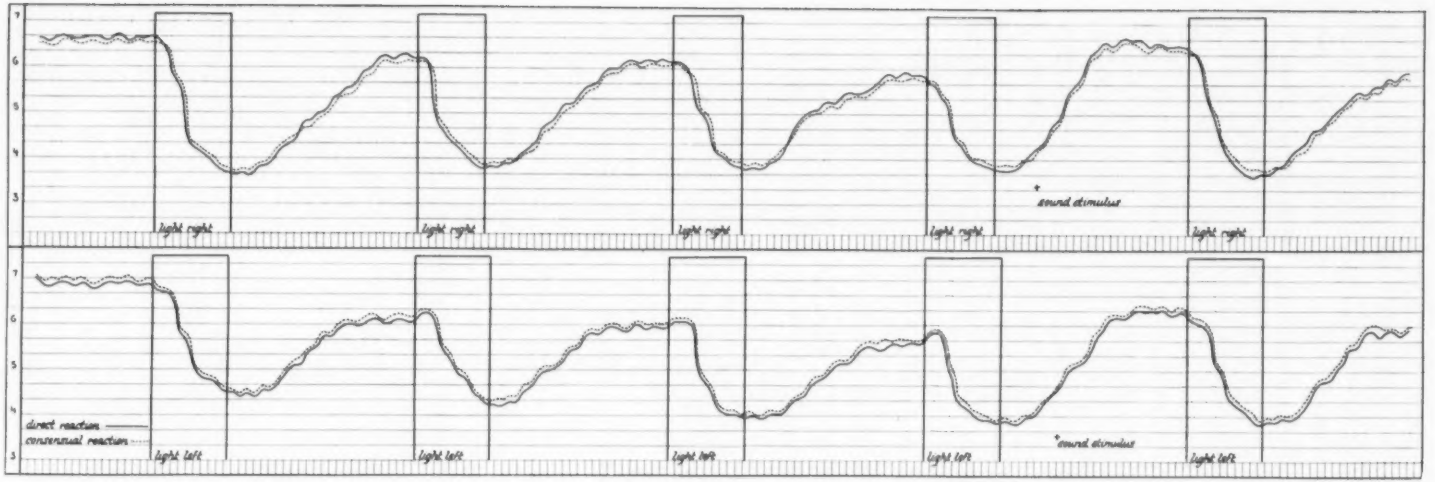

Fig. 12.—Asymmetric fatigue symptoms present only in the reflex to light of the left pupil in the preclinical stage of a syphilitic lesion of the central nervous system (the second reaction on the left side shows the initial dilatation).

to light of the left pupil did not disappear. As a matter of fact the treatment which improved the reaction of the left pupil so far as the premature initial dilation was concerned could not achieve a normal reaction so far as the prolonged latency period was concerned.

Figure 13 is the pupillogram of a patient with much more advanced tabes dorsalis. It reveals a good reaction to light on the left side and a sluggish and small reaction on the right side. After four light stimulations of the right side the pupil was exhausted and almost immobile; a sound stimulus, however, provoked a good psychosensory restitution effect. As a matter of fact, in this case antisyphilitic treatment resulted in a good restoration of the light reflex of the right pupil, the reflex becoming approximately like the fifth reaction in figure 13. The psychosensory restitution phenomenon under pathologic conditions is effective as long as the tissues involved in the function are not destroyed. As soon as they are destroyed the phenomenon disappears.

The degree of the psychosensory restitution effect is indicative of the state of the tissues involved and therefore contains important indications for the prognosis. The stages of reactivity existing for a longer or for a shorter time while the tissue is regenerating are analogous to those transient stages through which the function is carried in physiologic recovery by means of the psychosensory restitution phenomenon.

The analogy which exists between fatigue and degeneration also exists between recovery and regeneration. It is in harmony with a general biologic principle.

Psychosensory restitution, as may also be mentioned, is not limited to the pupillary phenomena. Since a sympathetic reflex is involved, it extends as far as the sympathetic system itself; that is to say, it governs the state and the function of all tissues, particularly the muscle tissues (Orbeli effect). It is not, as was formerly supposed, exclusively a recovery phenomenon but, as can be shown both in animals [7] and in man, governs rather the facilitation and the deepening of all functions. As a restitution phenomenon it is in principle the recovery of the body awake. As a vegetative sympathetic reflex, the psychosensory restitution phenomenon is capable of fatigue, like another sympathetic reflex, the reflex to darkness. In this case the parasympathetic portion of the vegetative system becomes dominant, the pupils become small, the heart rate decreases, the blood pressure falls and the body falls asleep.

ANISOCORIA; CONVERGENCE AND DIVERGENCE IN THE PUPILLOGRAPHIC PICTURE

We have emphasized that normally the right and the left pupil have the same size and maintain the same size during the reaction to stimuli, that is to say that direct and consensual reactions are identical for all

7. Experiments to be published in collaboration with M. B. Bender.

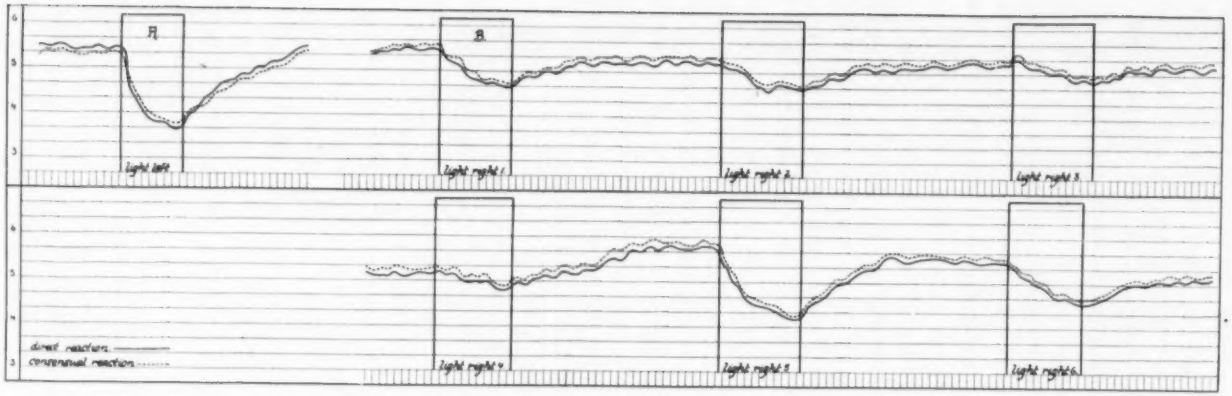

Fig. 13.—Psychosensory restitution phenomenon in a case of advanced tabes dorsalis. The reaction to light was good on the left side (*A*) and sluggish and small on the right side (*B*). The reflex to light on the right side was exhausted after four stimulations but well restored by a sensory (sound) stimulus (fifth reflex to light).

pupillary responses. Differences in size are called anisocoria. We call anisocoria which exists before a stimulus has induced a movement static anisocoria and that which exists only during a reaction dynamic anisocoria. Dynamic anisocoria may occur either during contraction or during dilation.

Static anisocoria may be due either to a sympathetic or to a parasympathetic lesion. Dynamic anisocoria of the dilation phase is generally due to a lesion within the sympathetic part of the reflex arc. Anisocoria occurring or increasing during contraction is generally due to a lesion in the parasympathetic fibers unless the subject is under the influence of cocaine. Static anisocoria of sympathetic origin tends to diminish during contraction. Static anisocoria of parasympathetic origin has a tendency to increase during contraction.

When static anisocoria is caused by a lesion either in the third or in the second sympathetic neuron, contraction will not be hindered on the side of the lesion; it is characteristic of this kind of sympathetic anisocoria that in contraction it will be diminished or at least will maintain its former degree. But during the dilation phase this kind of anisocoria will increase. It will also increase in reactions to darkness and to psychosensory stimuli, but the psychosensory restitution phenomenon will be diminished on the side of the lesion. In association with a lesion of the third neuron, there will also be a dilation in response to epinephrine although not in response to cocaine; whereas in association with a lesion in the second neuron, there will be a dilation in response neither to cocaine nor to epinephrine. A lesion in the first neuron may have one of two different features; it may either produce a miosis (if the lesion is a sympathetic paralysis) or a mydriasis, as in Adie's syndrome, in which a central sympathetic irritation is involved. The former lesion produces the Horner syndrome: The pupil dilates in response to cocaine and to psychosensory stimuli, but the psychosensory restitution phenomenon is absent and there frequently are tonohaptic reactions. In cases of irritation one must distinguish between an irritation of greater or of lesser degree. In the cases of irritation of lesser degree, the psychosensory dilation is increased; the psychosensory restitution phenomenon is also increased but is easily fatigued. In cases of irritation of greater degree, the pupil no longer reacts to light but recovers the ability to react to light under the influence of physostigmine.[8] The dilation in response to psychosensory stimuli is diminished but present, and the psychosensory restitution phenomenon is absent. There are regularly tonohaptic reactions also on the side contralateral to the lesion.

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8. Löwenstein, O.: L'importance de l'épreuve à l'éserine pour le diagnostic différential entre le pseudo-tabès pupillotonique (Adie) et le tabès, Schweiz. med. Wchnschr. **69**:377, 1939.

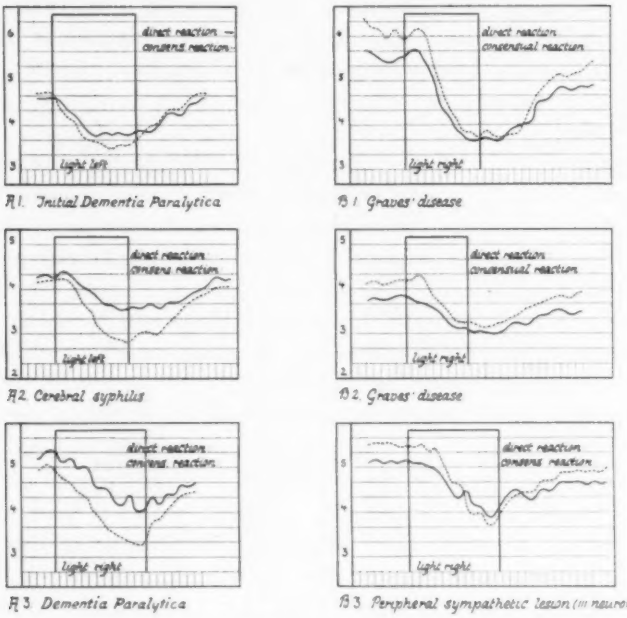

Fig. 14.—The "phenomenon of divergence and convergence"; the differential diagnosis between syphilitic and nonsyphilitic lesions of the central nervous system.

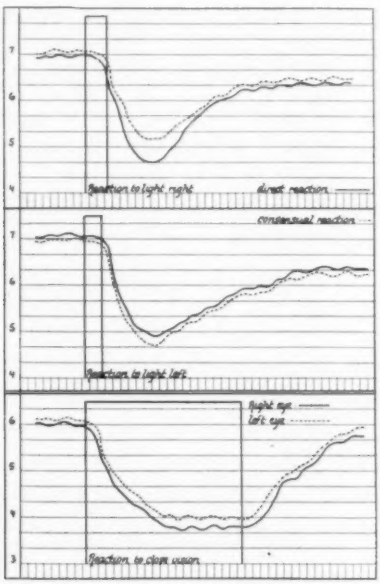

Fig. 15.—Dynamic anisocoria in the contraction phase of the reflex to light; syphilitic causation.

Anisocoria which is due to a lesion of the third nerve may be characterized by either a larger or a smaller pupil on the side of the lesion. A large pupil is due to a lesion between the third nerve nucleus and the periphery. If the lesion is complete, a reaction to physostigmine no longer occurs. If the pupil is small, the condition must be due to a supranuclear lesion. We are generally able to find such a lesion by eliciting a reflex to light, since it is characterized by a more or less pronounced dynamic anisocoria in the pupillographic picture.

Anisocoria which is due to a sympathetic lesion is generally not of syphilitic origin. Anisocoria located in the parasympathetic nerve, however, is frequently syphilitic. These statements hold only for acquired syphilis; congenital syphilis may give rise to lesions in the sympathetic nerve, in the parasympathetic nerve or in both.

If one traces pupillographically (fig. 14) the differences between small lesions in the third nerve and small lesions in the sympathetic nerve (except for irritative central sympathetic lesions) one finds converging graphs in the case of sympathetic lesions and diverging graphs in the case of parasympathetic lesions. Diverging graphs are generally found in association with a lesion of syphilitic origin and converging graphs in association with a nonsyphilitic lesion. This fact was designated "the phenomenon of convergence and divergence" (Francheschetti and Löwenstein). It permits one to distinguish easily between these types of lesions.

Dynamic anisocoria in the contraction phase, as shown in figure 15, is a valuable sign in the early diagnosis of lesions which in adults are nearly always due to syphilis.

SUMMARY

We have tried to show what pupillography has thus far accomplished both in general research and in the diagnosis of early lesions of the central nervous system. As to further details and particularly as to the experiments from which issued the results mentioned, we refer the reader to the original publications of the senior author.

RESECTION OF LEVATOR PALPEBRAE MUSCLE BY THE CONJUNCTIVAL ROUTE FOR PTOSIS

SIMPLIFIED TECHNIC

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Resection of the levator palpebrae muscle by the conjunctival route, described by de Blaskovics [1] in 1923 and 1929, soon became popular in this country. While good results were obtained, the effect of the operation in some cases was disappointing. I was convinced that the poor results were due to faulty technic. In my attempt to simplify the operation, I succeeded in getting not only good corrections but even overcorrections. These results were obtained even when apparently there was no action in the levator muscle before the operation. The effect was seemingly mechanical. This fact was mentioned by de Blaskovics.

It is because I believe that the slight variations in technic facilitate the operation, so that the steps are easier to follow, that I feel justified in making this report. The operation is similar to tarsal resection but is more effective, because the levator tendon, with its relation to surrounding structures, plays an important role.

Anatomically speaking, the insertion of the levator tendon consists of two main layers. One is attached to the upper margin of the tarsus; the other, to the anterior surface of the lower third of the tarsus. The first, or inner, layer, which is attached to the margin of the tarsus, has Müller's smooth muscle incorporated in it. Anterior to the levator tendon are the orbicularis muscle and the skin, and posterior to it is the conjunctiva.

TECHNIC

1. Pontocaine or cocaine solution is instilled.

2. The eyelid is injected with 2 per cent procaine hydrochloride solution.

3. The upper lid is grasped with an Ehrhardt clamp forceps and everted as for tarsal resection.

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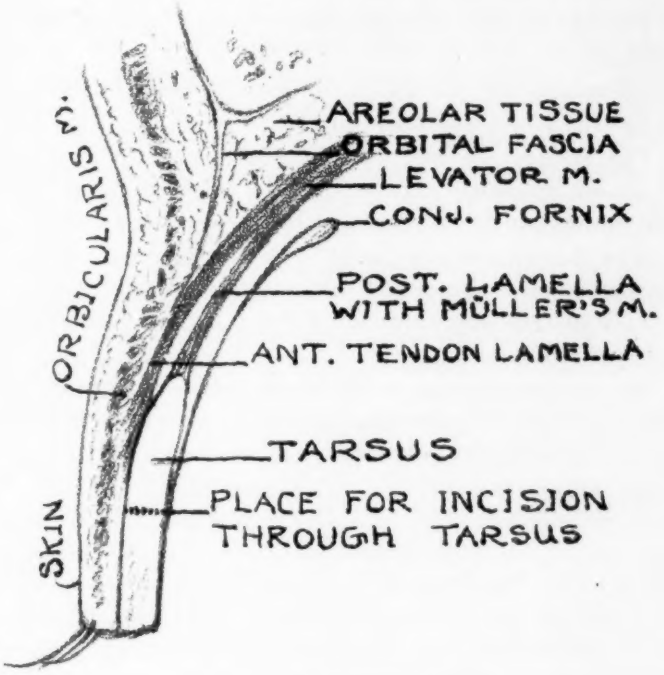
1. de Blaskovics, L.: A New Operation for Ptosis with Shortening of the Levator and Tarsus, Arch. Ophth. **53**:563-573 (Nov.) 1923; Treatment of Ptosis: Formation of Fold in Eyelid and Resection of Levator and Tarsus, ibid. **1**:672-680 (June) 1929.

4. With a scalpel the operator cuts through the tarsus, clear across, 3 mm. below the upper margin. He should exercise care not to cut through the anterior layer of the levator tendon. A clean cut through the tarsus brings into view the pretarsal space behind the levator tendon. Dull dissection will free the tarsus up to the upper margin.

5. At this point further dull dissection would separate Müller's muscle from the anterior lamella of the tendon. It is, however, inadvisable to separate the two lamellas. By cutting through the attachment of the posterior lamella to the upper margin of the tarsus, the conjunctiva



Insertion of the levator tendon.

is dissected free of the two layers of the levator tendon, which remain in close contact with each other.

6. Holding the cut tarsus on tension, the operator continues a clean dissection of the conjunctiva up to the fornix until loose areolar tissue behind the muscle is reached.

7. The posterior surface of the combined muscle-tendon is now facing the operator. It is picked up with a forceps near the lower cut edge of the tarsus. A careful nick will expose the anterior line of cleavage between the levator tendon and the orbicularis muscle. The tendon is

then slit across parallel to the cut edge of the tarsus. Along the line of cleavage, the broad tendon is dissected from the posterior surface of the orbicularis until again areolar tissue is reached and thus the membranous tendon freed.

8. Three double-armed sutures are passed through with the loop on the inner surface, one central and two lateral. (No. 5 twisted or no. 2 braided silk sutures are used.) The level of these sutures determines the degree of resection. The higher on the tendon the sutures are placed the stronger is the effect.

9. The tendon is then resected 2.5 mm. below the sutures.

10. The conjunctiva, with the resected tarsus, is sliced off at a corresponding level.

11. All needles are now passed through between the tarsus and the skin, to emerge 2 mm. above the lid margin.

12. The sutures are tied over a small gauze roll. Conjunctival sutures are not absolutely necessary, as the conjunctiva falls into place. Separate sutures can be introduced at the end of the operation.

13. With the retraction of the lid by this operation, the fold in the lid forms spontaneously. To insure this fold, the operator may choose to pass a single basting suture through the skin and the orbicularis muscle at the proper level.

14. The conjunctival sac is filled with sterile petrolatum. A cone dressing is applied. The dressing should be removed after twenty-four hours and only protective petrolatum used.

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PENETRATION OF SULFATHIAZOLE INTO THE EYE

FURTHER STUDIES

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AND
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Previous studies [1] reported from this department have shown that sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) after oral administration to cats appears in the aqueous of normal eyes in relatively small quantities. Only 18.4 per cent as much was found in the aqueous as in the blood. On the other hand, sulfanilamide, sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine) and sulfadiazine (2-[paraaminobenzenesulfonamido]-pyrimidine) attained the high level in the aqueous of 75 to 80 per cent of the level in the blood. Bellows and Chinn [2] obtained similar results in dogs. Liebman and Newman,[3] working with rabbits, reported comparable data. Because of the low concentrations of sulfathiazole in the ocular tissues it was implied that clinical use of the substance against intraocular infections was probably inadvisable.

Such a restriction of the use of sulfathiazole would be unfortunate, since this drug has certain advantages over other sulfanilamide compounds. It ranks low in toxicity. It is the drug of choice in combating staphylococcic and gonococcic infections and possesses a rather wide range of effectiveness against other organisms.

In the presence of intraocular infections and external irritative processes, especially those involving the cornea, the protein content of the aqueous humor is considerably increased. The severity of the condition may be such as to produce a coagulum of fibrin in the anterior

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Read before the Section on Ophthalmology, College of Physicians, Feb. 19, 1942.

From the Department of Ophthalmology, University of Pennsylvania School of Medicine.

This work was made possible by a grant from the Smith, Kline & French Laboratories for study of the microcrystalline form of sulfanilamide and its derivatives.

1. Scheie, H. G., and Souders, B. F.: Penetration of Sulfanilamide and Its Derivatives into Aqueous Humor of the Eye, Arch. Ophth. **25**:1025 (June) 1941.

2. Bellows, J. G., and Chinn, H.: Penetration of Sulfathiazole in the Eye, Arch. Ophth. **25**:294 (Feb.) 1941.

3. Liebman, S. D., and Newman, E. H.: Distribution of Sulfanilamide and Its Derivatives Between Blood and Aqueous, Arch. Ophth. **26**:472 (Sept.) 1941.

chamber. This possibility has long been known and has been attributed to a change in the permeability of the intraocular blood vessels resulting from the direct action of toxins and through axon reflexes. With this fact in mind, we considered it possible that sulfathiazole might likewise be present in the aqueous to a greater degree under similar conditions, so the following experiments were undertaken.

Sulfathiazole [4] in the microcrystalline form was employed in all our experiments.[5] This preparation consists of a suspension of sulfathiazole crystals 5 to 10 microns in diameter suspended in a neutral solution. The size of the crystal is such that it will readily pass through a no. 26 needle; thereby it possesses many advantages in administration, particularly by injection. At the present time studies are being carried out to determine any therapeutic advantages the drug may have. Our first step was to compare its rate and degree of penetration with those of ordinary preparations of the drug.

METHOD OF STUDY

Cats were used in all the experiments. Anesthesia was obtained with sodium amytal, 50 mg. per kilogram of body weight given intraperitoneally. The preparation used was the microcrystalline form of sulfathiazole. In all the experiments administration was by the intraperitoneal route. All specimens of blood were taken by cardiac puncture. Specimens of aqueous were obtained by limbal puncture as nearly simultaneously as possible. In producing infection a standardized laboratory strain of Streptococcus (hemolytic) was used. Chemical analyses [6] were performed by the method of Bratton and Marshall.[7]

EXPERIMENTS

Series 1.—Animals with normal eyes were given 200 mg. of microcrystalline sulfathiazole per kilogram of body weight intraperitoneally. Samples of blood and aqueous were taken six hours later. Analyses revealed (table 1) that the aqueous contained about 24 per cent as much sulfathiazole as the blood, a percentage which was comparable to that previously found for ordinary sodium sulfathiazole given orally. As a consequence we can conclude that the data recorded in the experiments to be described in this paper are applicable to either form.

Series 2.—Animals were inoculated with 0.02 cc. of the streptococcus culture into the vitreous. Sixteen hours later they were given microcrystalline sulfathiazole, 200 mg. per kilogram of body weight. At this time they were seen to have an overwhelming infection of the vitreous, as evidenced by marked conjunctival congestion, chemosis, miosis and haziness of the vitreous. Six hours later specimens of blood and aqueous were taken. In some of the animals clots of fibrin were

4. Chambers, L. A.; Calkins, H. E., and Souders, B. F.: Preparation of the Microcrystalline Form of Sulfanilamide and Its Derivatives, unpublished data.

5. Prepared by the Smith, Kline & French Laboratories.

6. All analyses were done by D. A. Stevens in the laboratory of the Children's Hospital.

7. Bratton, H. G., and Marshall, E. K., Jr.: New Coupling Component for Sulfanilamide Determination, J. Biol. Chem. **128**:537 (May) 1939.

present in the anterior chamber. In cat 5 no aqueous was obtained, because of a coagulum, so vitreous was aspirated. The results (table 2), showing a mean level in the aqueous of 91 per cent of that in the blood, revealed a great increase in the concentration of sulfathiazole over that in normal eyes. This was even considerably above the values noted for secondary aqueous in our previous report. The content in the specimen of vitreous was also elevated (42 per cent), though showing a lag behind that in the aqueous.

TABLE 1.—*Blood and Aqueous Content of Sulfathiazole in Cats with Normal Eyes Six Hours After Microcrystalline Sulfathiazole, 200 Mg. per Kilogram of Body Weight, Had Been Injected*

Cat	Concentration in Blood, Mg. per 100 Cc.	Eye	Concentration in Aqueous, Mg. per 100 Cc.	Sulfathiazole, Aqueous-Blood, Percentage
1	18.29	Right	4.59	25.0
		Left	4.48	24.4
2	12.35	Right	3.23	26.1
		Left	3.10	25.0
3	13.73	Right	3.23	23.5
4	17.83	Right	4.72	26.4
		Left	4.09	22.9
5	16.83	Right	3.99	24.4
		Left	4.00	24.4
6	26.73	Right	6.23	23.3
7	10.17	Right	2.33	22.9
8	18.68	Left	4.62	24.7

TABLE 2.—*Penetration of Sulfathiazole into the Aqueous of Cats' Eyes Infected by Injection into the Vitreous of 0.02 Cc. of a Culture of Hemolytic Streptococci* *

Cat	Concentration in Blood, Mg. per 100 Cc.	Concentration in Aqueous, Mg. per 100 Cc.	Sulfathiazole, Aqueous-Blood, Percentage
1	6.14	5.41	88
2	7.9	7.9	100
3	10.49	7.79	74
4	14.26	15.5	108
5	14.72	12.6 (right) 6.27 (left) in vitreous	85 42 in vitreous

* Sixteen hours later microcrystalline sulfathiazole, 200 mg. per kilogram of body weight, was given intraperitoneally, and samples of blood and aqueous were taken simultaneously six hours after administration of the drug.

SERIES 3.—The experiments were done similarly to those in the preceding series. The animals were inoculated with 0.01 cc. of the culture in an attempt to produce a milder infection if possible. For the same reason the sulfathiazole was given only three hours after the infection was produced. Specimens of blood and aqueous were taken six hours later. Even with these precautions the eyes showed marked inflammatory reactions, though slightly milder than those in series 2. The specimens of aqueous (table 3) contained somewhat less sulfathiazole than those from the animals of series 2, which were suffering from more severe infections. The mean value for the aqueous was 82 per cent of that for the blood.

SERIES 4.—Attempts were made in 2 animals to reduce further the severity of the infection by injecting a smaller number of organisms (0.005 cc. of the culture) and by giving the sulfathiazole simultaneously. However, severe infection resulted, which caused the levels of sulfathiazole in the aqueous to be high, approximating those in series 3.

TABLE 3.—*Penetration of Sulfathiazole into the Aqueous of Cats' Eyes Infected by Injection into the Vitreous of 0.01 Cc. of a Culture of Hemolytic Streptococci* *

Cat	Concentration in Blood, Mg. per 100 Cc.	Eye	Concentration in Aqueous, Mg. per 100 Cc.	Sulfathiazole, Aqueous-Blood, Percentage
6	3.83	Right	3.23	94
		Left	3.76	98
7	15.25	Right	7.85	51
		Left	13.86	90
8	5.68	Right	4.62	81
		Left	4.48	78
9	5.02	Right	4.55	90
		Left	4.42	88
10	8.73	Right	6.47	77
		Left	7.39	82
11	7.06	Right	5.68	80
		Left	6.27	88

* Three hours later microcrystalline sulfathiazole, 200 mg. per kilogram of body weight, was given intraperitoneally, and samples of blood and aqueous were taken simultaneously six hours after administration of the drug.

TABLE 4.—*Changes in the Distribution of Sulfathiazole Between the Blood and the Aqueous Following Injection Subconjunctivally and into the Vitreous of Mecholyl Hydrochloride and Histamine*

Cat	Drug	Concentration in Blood, Mg. per 100 Cc.	Eye	Concentration in Aqueous, Mg. per 100 Cc.	Sulfathiazole, Aqueous-Blood, Percentage
14	Mecholyl subconjunctivally	11.56	Right	3.23	27.9
			Left	3.3	28.5
17	Mecholyl into vitreous	12.34	Right	4.48	36.2
			Left	4.75	38.4
15	Histamine subconjunctivally	12.54	Right	3.7	29.5
			Left	3.17	25.2
16	Histamine into vitreous	9.50	Right	4.42	52.8
			Left	5.02	46.5

SERIES 5.—In 2 animals 0.005 cc. of the culture of hemolytic streptococci was injected intracorneally. At the same time the usual amount of sulfathiazole was injected intraperitoneally. The first specimens of blood and aqueous were taken six hours later. Ulcers about 3.5 mm. in diameter that were never extremely severe developed. Their course was mild, and they gradually healed over a period of seven days with continued daily intraperitoneal injections of sulfathiazole, 200 mg. per kilogram of body weight. Specimens of blood and aqueous were taken periodically to make it possible to follow the sulfathiazole levels as the eyes healed. The intervals after the first six hours were forty-eight hours and one week. As can be seen in chart 1, the percentage of sulfathiazole in the aqueous diminished with healing of the ulcers.

SERIES 6.—To obtain relatively isolated effects of vasodilatation in the absence of inflammation, mecholyl hydrochloride 0.25 mg. and histamine 0.25 mg. were injected subconjunctivally into the eyes of separate animals which had been given the usual amount of sulfathiazole intraperitoneally six hours before. Specimens of blood and aqueous were taken two hours after the medication was given. The aqueous contained (table 4) about 30 per cent as much sulfathiazole as the blood, or 6 per cent more than the mean level for normal eyes. In 2 animals the same amount of the drugs was injected into the vitreous. The histamine increased the sulfathiazole content of the aqueous more than did mecholyl. The eyes given histamine showed more chemosis and reaction and the aqueous contained 49.6 per cent as much sulfathiazole as the blood, while the eyes given mecholyl showed less reaction and the aqueous contained 37 per cent as much drug as the blood.

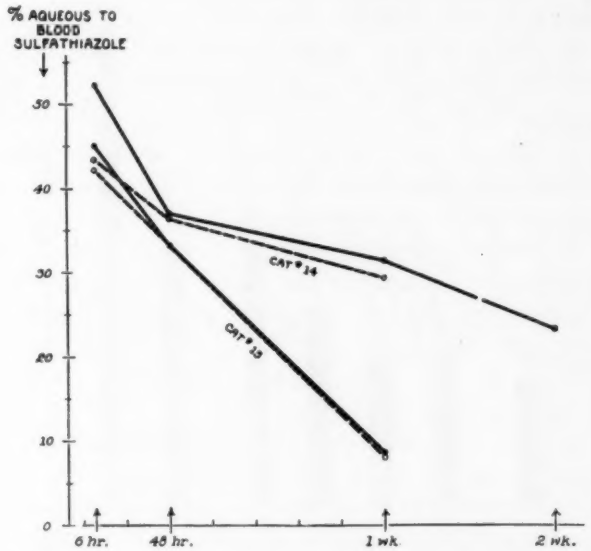

Chart 1.—Curves showing the falling values for sulfathiazole in the aqueous as corneal ulcers heal and the eyes are quiet over a period of two weeks. The corneas were infected by intracorneal injection of 0.005 cc. of a culture of hemolytic streptococci. Sulfathiazole, 200 mg. per kilogram of body weight, was administered simultaneously and was subsequently injected daily.

Therefore, the values for sulfathiazole were higher for the eyes showing the more chemosis and vasomotor reaction, though produced in a different manner.

COMMENT

Experiments have been described which show the penetration of sulfathiazole into the aqueous of cats' eyes with varying degrees of inflammatory and vasomotor reactions. A new type of sulfathiazole was used in the experiments, a microcrystalline preparation. Preliminary studies showed that excellent levels of sulfathiazole in the blood resulted from intraperitoneal injection and that penetration into the aqueous of normal eyes was comparable to that in previous studies with sodium

sulfathiazole given orally. The bacteriostatic and chemical properties of the microcrystalline form are known to be the same as those of ordinary preparations. Because of the ease of administration and the good levels in the blood obtained, it was used throughout these experiments.

The blood-aqueous ratio of sulfathiazole was found to be entirely different in eyes with experimental infections. Specimens of aqueous from such eyes showed sulfathiazole levels (chart 2) proportionate to the severity of the inflammatory reactions. Eyes with fulminating experimental abscesses of the vitreous yielded aqueous containing, as the

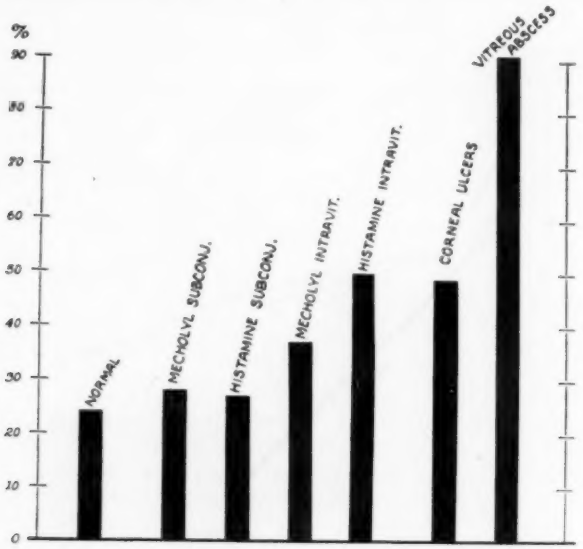

Chart 2.—Comparison of the influence of mecholyl hydrochloride, histamine and infection on the intraocular penetration of sulfathiazole.

mean level, 91 per cent as much sulfathiazole as the blood. A second series of animals, with somewhat milder infections of the vitreous, showed a mean level 82 per cent of that of the blood. For eyes with moderately severe corneal ulcers the aqueous-blood percentage of sulfathiazole was 46 when the ulcers were acute, gradually diminishing as the ulcers healed.

Since infection dilates vessels and increases their permeability by toxic action, an attempt was made to increase the sulfathiazole content of the aqueous by pharmacologic means. The drugs of choice were a choline derivative, mecholyl hydrochloride, and histamine. Both substances are vasodilators, with histamine affecting mainly the capillaries, greatly increasing their permeability, which results in intense transudation according to Duke-Elder.[8]

8. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1932, vol. 1, p. 422.

Friedenwald [9] showed that histamine injected into the vitreous of a dog resulted in plasmoid aqueous owing to a partial destruction of the osmotic barrier between plasma and aqueous. In studies with mecholyl instilled locally onto the cornea, Swan [10] showed that the protein content of the aqueous was increased, which fact he attributed to an increase in the permeability of the blood-aqueous barrier. He found that the size of the pupil had no effect. We injected the substances in different animals beneath the conjunctiva and into the vitreous. Mecholyl hydrochloride and histamine produced marked dilatation of the conjunctival vessels, with extreme edema resulting in the eyes given histamine. Each drug increased the sulfathiazole content of the aqueous to 30 per cent of that of the blood (chart 2). Mecholyl hydrochloride injected into the vitreous produced marked miosis and moderate hyperemia of the conjunctiva. Aqueous from the eyes given mecholyl contained 37 per cent as much sulfathiazole as the blood.

Histamine injected into the vitreous again produced marked conjunctival edema but decreased the pupil only slightly in size. The volume of the anterior chamber was increased. The aqueous was found to contain 50 per cent as much sulfathiazole as the blood.

No attempt is made to draw any conclusions from these experiments as to the mechanism of the production of aqueous. It does seem, however, of sufficient interest to warrant mentioning that the penetration of sulfathiazole into the eye parallels the behavior of serum proteins. Like serum proteins, the drug cannot freely enter the aqueous, for it is probably held back by the blood-aqueous barrier, which acts as a semipermeable membrane. This barrier seems closely related in function to the capillary bed of the eye, for, as is well known, vasodilator substances increase its permeability, allowing such molecules as protein to pass into the aqueous. It is probably in this way that infection causes the sulfathiazole content of the aqueous to be high. Why sulfathiazole should be held back is not known, for its molecular size is comparable to that of sulfapyridine and of sulfadiazine. In view of its behavior in our experiments, the explanation may well lie in its molecules being bound to larger molecules.

Clinical application of the knowledge of the increased penetration of sulfathiazole into the aqueous of infected eyes is of considerable importance. When its use is indicated by the nature of the infection, one can employ it knowing that concentrations in the infected ocular

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9. Friedenwald, J. S., and Pierce, H. F.: Circulation of the Aqueous, Arch. Ophth. **8**:9 (July) 1932.

10. Swan, K. C., and Hart, W. M.: A Comparative Study of the Effects of Mecholyl, Doryl, Eserine, Pilocarpine, Atropine, and Epinephrine on the Blood-Aqueous Barrier, Am. J. Ophth. **23**:1311 (Dec.) 1940.

fluids should be adequate, though studies on human eyes would be desirable.

This statement is given further support by recent reports of the therapeutic effectiveness of sulfathiazole against meningitis. These reports add weight because of the similarity of aqueous and spinal fluid in composition and also because it is likely they have a similar mechanism of production. At any rate, the sulfathiazole content of normal spinal fluid is about the same as that of normal aqueous humor. Sadusk and Blake [11] found only traces of sulfathiazole to 18 per cent of the content in the blood in human beings. Bellows and Chinn,[2] working with dogs, found the content in the spinal fluid and that in the aqueous to be low and approximately equal. Because of these low values, sulfathiazole has in the past seldom been used in the treatment of meningitis, and in fact admonitions [12] have been made against its employment.

At the present time reports of its use are beginning to reach the literature, such as that by Banks,[13] who treated 96 patients with epidemic meningitis with only a 2 per cent mortality. He found the sulfathiazole content, in his few analyses of abnormal spinal fluid, to be 15 to 40 per cent of that in the blood. Carey [12] reported ratios of 10 to 25 per cent. None of these observers commented on the elevation of the sulfathiazole level in the spinal fluid of their patients, but it seems plausible that the therapeutic value of the drug might be due to the increased penetration through inflamed meninges. However, other factors must be considered, since in meningitis the infection is probably primarily in the meninges, with the spinal fluid showing only secondary changes. In the eye, on the other hand, any purulent infection rapidly develops in the culture medium offered by the vitreous, and the antibacterial substance must reach a good level in this tissue before it will be effective.

CONCLUSIONS

1. Microcrystalline sulfathiazole enters the aqueous humor of the normal cat's eye in small quantities, comparable to those of ordinary sulfathiazole.

2. Penetration of sulfathiazole into the aqueous is greatly increased by ocular inflammation and by vasodilator drugs.

3. Until further evidence is accumulated, its use against ocular infections is probably not contraindicated.

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11. Sadusk, J. F., Jr.; Blake, F. G., and Seymour, A.: Observations on the Absorption, Excretion, Diffusion and Acetylation of Sulfathiazole in Man, Yale J. Biol. & Med. **12**:681 (July) 1940.

12. Carey, B. W.: Use of Sulfanilamide and Related Compounds in Diseases of Infancy and Childhood, J. A. M. A. **115**:924 (Sept. 14) 1940.

13. Banks, H. S.: Sulphathiazole in Cerebrospinal Fever, Lancet **1**:104 (Jan. 25) 1941.

DUPLEX ROD WITH HANDLE FOR ROUTINE INVESTIGATION OF EXTRAOCULAR MUSCLES

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As White has frequently pointed out, the determination of the type and the degree of heterophoria in the primary position, for distance and for near vision, is meaningless from the diagnostic standpoint unless the behavior of the individual ocular muscles is studied in the different cardinal positions of gaze: up and right, right, down and right, up and left, left and down and left. It is only through this examining procedure that paralyses of the extraocular muscles can be accurately diagnosed and the motor anomalies they produce clearly differentiated from purely innervational disturbances of the convergence and divergence centers.

Unfortunately, in daily practice the routine investigation of the extraocular muscles is frequently done in the primary position only, for distance and near, with the Maddox rod. Owing to pressure of time or lack of familiarity with the screen test and prism measurements, the diagnostic positions of gaze are studied only in those cases in which an obvious motor anomaly is present. However, individual muscular overaction and underaction, particularly of the vertical rectus and the oblique muscles, while giving rise to considerable asthenopia, may not cause any heterophoria in the primary position, the deviation being present only in the field of action of the affected muscle. It is apparent, therefore, that the diagnosis is entirely missed or overlooked.

Since the Maddox rod test is the most commonly used and the best known routine procedure for the investigation of heterophorias by the average ophthalmologist, I have had made[1] two large multiple red rods about 65 mm. in diameter mounted on the ends of a bakelite handle 15 cm. long (fig. 1). These multiple rods are oriented in a direction perpendicular and parallel, respectively, to the handle, so that each of them may be held alternately in front of the eye to make the position of the red line image suitable for the study of horizontal and vertical imbalances (fig. 2).

The large size of the duplex rod makes it simple and easy to test the eyes not only in the primary positions but—and this is the main

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1. By the American Optical Company, Southbridge, Mass.

purpose of the instrument—in the six diagnostic positions, which can be done only with considerable difficulty with the small size Maddox rod found in trial cases.

In the study of the muscle balance in the primary position at 6 meters, the ordinary muscle light, 1 cm. in diameter, which is found in most illuminated chart cabinets, is used, the patient holding the duplex rod

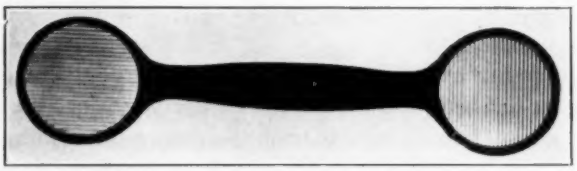

Fig. 1.—Duplex rod with handle.

Fig. 2.—Duplex rod in place for investigation of vertical imbalance in the diagnostic positions of the gaze.

in front of one eye. The type of vertical and horizontal heterophoria, if present, is thus determined and its degree measured in the usual manner, by putting prisms in front of the other eye until the red line crosses the light. The test for near vision is similarly done, with the light of an ophthalmoscope from which the head has been removed, or any other suitable small light, held in the midline 33 cm. from the

eyes. One should determine the muscle balance with and without glasses in order to find what influence the optical correction may have on the heterophoria present. For this purpose there is a distinct advantage of the duplex rod over the small Maddox rod of the trial case; the latter has to be inserted in the cell of the trial frame, while the former is simply held by the handle in front of it. This convenience is better appreciated when there is a cylindric lens in the correction and the rod must be rotated 90 degrees to change the red line image from the vertical to the horizontal position, or vice versa.

Once the muscle balance has been investigated in the primary position for distance and for near vision, the duplex rod is used in the six diagnostic positions, the light being held about 33 cm. from the eyes. The type of imbalance is thus determined in each position and its degree measured with prisms. Since the measurements are only relative and vary with the distance at which the light is held, it is

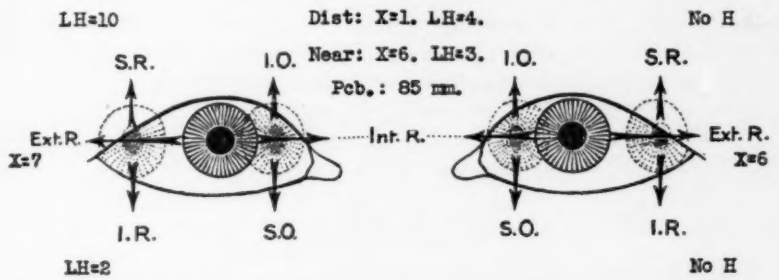

Fig. 3.—Dr. James W. White's diagnostic card, illustrating the method of recording the findings with the duplex rod in a case of paralysis of the right superior rectus muscle. *X* indicates exophoria; *H*, hyperphoria, and *LH*, left hyperphoria.

important that this distance be always the same in the different positions at which the test is conducted.

When the light is held in the oblique positions there is a slight distortion of the red line, which appears somewhat curved, but this does not interfere with the accuracy of the test, as the line will always cross the light when orthophoria is present. In cases of heterophoria, the determination as to whether the imbalance, that is the distance separating the light and the red line, is constant or changes and the interpretation in the positions in which this distance is greatest will furnish a presumptive diagnosis as to the muscle or muscles involved, which, of course, should be corroborated by other tests. For practical purposes it suffices to measure solely the lateral imbalance in the positions right and left, for any hyperphoria present at these levels is irrelevant as far as the functional study of the lateral rotators is con-

cerned. On the other hand, the type and the measurement of the hyperphoria alone is all that is required in the upper and lower positions, up and right, down and right, up and left and down and left, for the investigation of the motility of the elevator and the depressor muscles.

A helpful aid in the interpretation of the test is White's diagnostic card, with its simple, clear diagram showing the two predominant muscles acting in each one of the six cardinal positions (fig. 3). A careful analysis of this card, with the findings recorded in the corresponding spaces, will identify the muscle or muscles involved, since in the position of maximal imbalance the eye that lags is the paretic eye.

In cases of strong fusional innervation, the duplex rod can also be used to great advantage in conjunction with the screen test, in which alternate occlusion of the eyes may uncover an imbalance not shown by the rod alone.

Bearing in mind the limitations of a subjective test, as well as those of the Maddox rod itself, I have found the duplex rod a valuable aid in the routine study of heterophorias. It is a handy, inexpensive instrument, useful for the detection of vertical imbalance, particularly of low degree, in the diagnostic positions of gaze.

136 East Sixty-Fourth Street.

Correspondence

FUSIONAL MOVEMENTS IN PERMANENT STRABISMUS

To the Editor:—A few comments on Dr. Burian's very valuable paper in the October 1941 issue (ARCH. OPHTH. **26:** 626, 1941) might be in order.

1. All the patients cited by him had old neglected strabismus. It is entirely possible that they would have responded differently had they been cared for properly from the onset and so given a chance to learn binocular vision. Dr. Burian's test is of great value in that it is one more proof of the final harmful effect of early neglect.

2. All the operations were tenotomies, after which neuromuscular functions cannot act in a normal way. Moreover, in no patient was the operation successful in paralleling the eyes. The patients operated on, like those not operated on, had no chance to learn binocular vision.

3. Like all complicated tests, Dr. Burian's cannot be used when most needed—on babies before it is too late.

4. In view of these facts I would suggest that Dr. Burian study three more series of patients:

A. A series having eyes paralleled in early life by glasses only and having vision approximately equal.

B. A series having strabismus which developed from phorias and having therefore at one time had good binocular vision.

C. A series having eyes paralleled by operative methods that do not reduce muscular power.

I have had many patients coming under each heading who to all ordinary tests have a pair of eyes—not simply a pair of apparently straight eyes.

Dr. Burian's more scientific methods will prove whether or not my idea is correct, and I feel sure that it will further prove the value of proper early care.

5. "Babies reaching for the moon" shows the absence of stereoscopic vision, which must be learned by experience, not by fusion training. Therefore, if the eyes are paralleled early in life the child learns in the normal way provided good vision has been retained in each eye by alternate monocular occlusion. I have seen this occur so often that I am disappointed when it does not occur.

RODERIC O'CONNOR, M.D., San Francisco.

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Cornea and Sclera

KERATOCONUS FOLLOWING CORNEAL TRANSPLANT. C. A. SWANSON, U. S. Nav. M. Bull. **39:** 549 (Oct.) 1941.

The first case of keratoconus as a sequel to corneal transplantation is recorded. The transplantation was performed by Castroviejo because of a central leukoma which reduced the vision to 0.1. The vision was improved by the operation to 0.8. Ensuing cyclitis, however, was followed by keratoconus, which reduced the vision to 0.1. The application of a contact glass restored the acuity to 20/20. J. E. LEBENSOHN.

A CASE OF BLUE SCLEROTICS. J. P. S. WALKER, Brit. J. Ophth. **25:** 383 (Aug.) 1941.

A woman aged 46 had blue scleras and deafness of the left ear of long standing and had suffered a fracture of the femur. There was no hereditary factor. The left eye was glaucomatous, and visual acuity was reduced to light perception. In a sclerocorneal trephine operation it required but one complete turn of the trephine to cut through. The case is reported to draw attention to the thinness of the sclera and to the absence of stretching of the sclera with considerably increased tension in an eye with so thin an outer coat. W. ZENTMAYER.

SULPHONAMIDE IN THE TREATMENT OF CORNEAL ULCER. A. PHILLIP and K. W. STUART, Brit. M. J. **2:** 336 (Sept. 6) 1941.

The authors have used the following preparation in a number of cases of serpiginous ulcer of the cornea: 5 cc. of 5 per cent azosulfamide solution in 30 cc. of petrolatum. The ointment was inserted into the conjunctival sac twice daily for a prolonged period. No other disinfectant was used. Unfortunately, in many cases of serpiginous ulcer there are other complications which have to be treated at the same time; so it is difficult always to say which of the various factors is responsible for the outcome. The authors have therefore compared two series of cases, one in which azosulfamide and one in which either mild protein silver or mercurochrome was used. On theoretic grounds local irradiation appeared well fitted to supplement the bacteriostatic action of the drug.

The authors believe that in their series the results of the treatment compared favorably with those of the orthodox treatment, though in the azosulfamide series the transparency of the resulting scar seemed to be definitely greater. The rapidity of the healing was the same in the two series, namely ten and one-half days.

The authors conclude that the results of treatment of serpiginous ulcer of the cornea by the application of azosulfamide ointment are encouraging, especially when the ointment is used in conjunction with the local application of ultraviolet light. ARNOLD KNAPP.

Experimental Pathology

OPHTHALMOLOGIC CHANGES DURING DEADLY BLEEDING AND REVIVAL OF DOGS. A. ASTAKHOVA, Vestnik oftal. **18:** 179, 1941.

The experiment was made on 10 dogs. Blood was let from the femoral artery until the respiratory and cardiac action stopped; five to ten minutes later an infusion of blood with dextrose and epinephrine was made by way of the femoral artery and vein.

The ophthalmoscopic changes observed first were a narrowing of the vessels and pallor of the disk; gradually the arteries became invisible and in the veins the current of blood was intermittent. The disk was pale, with distinct borders. This condition was observed ten to eleven minutes after the emptying of the body of blood and at the time of clinical death. Five to six minutes after the blood transfusion the disk had resumed its pinkish color and the retinal vessels filled with blood; in thirty to forty minutes they were normal. No hemorrhage or edema of the disk was observed during the experiment.

The intraocular pressure decreased to 8 mm. during the clinical death and returned to normal when the animal recovered. The pupils were dilated ad maximum at the time of death. The reaction of the pupils to light disappeared during the fifth or sixth minute after the experiment and reappeared in fifteen to twenty minutes after the beginning of the blood transfusion. The corneal reflex also disappeared during the experiment. The cornea was cloudy in the deep layers; evidently there was edema of the endothelium, as exfoliation of the epithelium was not observed. The lens remained transparent. O. SITCHEVSKA.

General Diseases

LOSS OF VISION FOLLOWING HAEMORRHAGE. H. L. TIDY, Brit. M. J. **1:** 774 (May 24) 1941.

The author speaks of the loss of vision after hemorrhage, a surprisingly rare complication of hemorrhage due to accident or trauma such as occurs in warfare. The mode of development of the disturbance of vision is of two types. In the first the disturbance follows closely or immediately after the hemorrhage. There are no changes in the fundus. The disturbance is transient; recovery begins immediately and is usually complete. The second type is more important. In this there is an interval after the hemorrhage before the vision is affected. The impairment may then advance for several days before recovery begins, and it is often permanent in some degree. The fundus changes are edema of the disk and of the retina. Optic nerve atrophy develops in the cases in which the impairment is permanent.

A short review of the literature is given, the articles of D. F. Harbridge (*Am. J. Ophth.* **7:** 192, 1924) and P. N. Panton (*Tr. Ophth. Soc. U. Kingdom* **55:** 47, 1935), in particular, being cited. The interval which elapses between the hemorrhage and the recognition of the impairment of vision is usually between three and eight days, though sometimes it is between eighteen and twenty days. The diminution of

vision may produce any stage from blurring to complete blindness. When vision is not lost the diminution may increase for three or four days and the vision then improve. Recovery may be rapid at first and then continue slowly for weeks or months. The upper part of the field of vision is less affected generally than the lower. The disturbance is usually bilateral. As to the final result, in 33 per cent of the cases blindness is complete and permanent and in 50 per cent there is no improvement from the maximum loss. In about 10 per cent good or complete vision is recovered. The field changes show great variations, and the ophthalmic changes are also inconstant. The principal change is edema of the disk and the retina, and the field changes are those suggestive of intoxication amblyopia (Goerlitz, M.: *Klin. Monatsbl. f. Augenh.* **64:** 764, 1920).

The essential pathologic lesion is presumably edema, with degeneration of the ganglion cells and subsequently optic nerve atrophy. Retrobulbar neuritis has also been suggested.

The following case was observed: A primipara aged 30 was confined on June 20, 1936. She had been anemic, and examination of the blood showed 3,500,000 red cells and a hemoglobin content of 50 per cent. Confinement was uneventful. The loss of blood was not sufficient to cause anxiety. Ten days later her mental condition, which was at first affected, had cleared up and the anemia was improved. She then complained that her vision was misty. She had bilateral central scotoma, and there was a 2 D. swelling of each disk without any other change. Four months later the vision had recovered completely and the fundi were normal.

ARNOLD KNAPP.

Glaucoma

INFLUENCE OF THE DARK ON THE BLINDSPOT AND ANGIOSCOTOMAS IN GLAUCOMA. A. DASHEWSKY, Vestnik oftal. **18:** 368, 1941.

Since the dark room test of Zeidel gives positive results in only one third of cases of glaucoma because of the inexactness of tonometry, Dashewsky decided to try out the dark room test and examine for changes in the blindspot and for angioscotomas in the early stages of glaucoma, when the tonometer frequently does not indicate an increase of the intraocular tension.

He examined 115 eyes in 59 patients. The blindspots, large angioscotomas and macular angioscotomas were examined carefully by Dashewsky's method. The patient then was put into a dark room for forty-five minutes, after which the threshold of sensitivity to light with a pupil 2 mm. wide was determined with Dashewsky's adaptometer; the blindspots and angioscotomas were again examined. Pilocarpine solution was still instilled. The patient again spent forty-five minutes in a dark room, and the functional tests were repeated. The following results were obtained:

Three groups of patients—one group having 30 eyes with chronic glaucoma, 20 patients with chronic glaucoma in one eye and prodromal glaucoma in the other eye and 9 patients (18 eyes) suspected of having

prodromal glaucoma—gave positive reactions to the pilocarpine test of adaptation and positive reactions to the pilocarpine angioscotometric test and the dark room angioscotometric test.

In the fourth group of patients (20 eyes), in which glaucoma was present in one eye in 3 patients, while in the other eye there was no suspicion of glaucoma, and in 14 eyes in which there were subjective signs, all the functional tests mentioned gave negative results. Negative results were also obtained in control eyes and in some patients who had enlarged blindspots and angioscotomas due to intoxication.

The field for blue was inverted in 68 per cent of cases.

These tests thus aid in the early diagnosis of glaucoma, before the tonometer registers an increase of intraocular tension.

O. SITCHEVSKA.

Lens

CATARACT EXTRACTION IN REFRACTORY PATIENTS AND OPERATIVE TREATMENT OF IRIDODIALYSIS. T. G. W. PARRY, Brit. J. Ophth. **25:** 553 (Dec.) 1941.

Parry describes a procedure for extraction of cataracts in refractory patients.

The method is a modified linear extraction. The lens is broken up with a knife-needle; later an iridectomy and extraction are made through a keratome incision. It has been found possible to break up even the nucleus with the knife-needle. The author had independently operated successfully for iridodialysis in the way previously described by Wheeler.

W. ZENTMAYER.

Lids

PALPEBRAL MANIFESTATIONS OF TERTIARY SYPHILIS. G. RENARD and P. HALBRON, Arch. d'opht. **2:** 599 (July) 1938.

Renard and Halbron present figures to show that tertiary syphilis of the lids is rare. They report on a patient who had first infectious blepharitis and then syphilitic ulceration. The exact nature of the disease was suspected because of the resistance to various types of treatment and was confirmed by serologic study. Treatment with iodides and mercurials resulted in a rapid cure. The authors point out that tertiary syphilis of the lids has many different characters. The conjunctiva may be attacked. Sometimes it is chemotic and infiltrated and forms a grayish flattened mass simulating a false membrane. The bulbar conjunctiva may be affected. The preauricular and submaxillary glands on the infected side become enlarged, hard and freely movable. Renard and Halbron point out that the disease of the lids may be associated with other stigmas of syphilis and with gumma elsewhere. Sometimes the palpebral gumma resembles chalazion. It is remarkable how completely and rapidly it is affected by treatment. Photographs of their patient reveal the progress of the condition.

S. B. MARLOW.

Methods of Examination

DISTANCE OBJECT TEST TYPE FOR CHILDREN. F. E. PRESTON, Brit. J. Ophth. **25:** 357 (Aug.) 1941.

Preston has constructed a test type chart on the strictly Snellen principle. An original test chart with thirty-two objects was printed and was tried out at school clinics in different parts of the country.

The objects retained are either easy to interpret or else capable of a varied interpretation, so that the test is an estimate of the child's visual acuity and not of his intelligence. The author recognizes that the same principle has been used before in the construction of test types for children.

W. ZENTMAYER.

THE HISTOLOGICAL INTERPRETATION OF APPEARANCES IN THE FUNDUS OCULI. A. J. BALLANTYNE, Brit. J. Ophth. **25:** 480 (Oct.) 1941.

This interesting article does not lend itself readily to abstracting.

The author states that there is a considerable gap between the ophthalmoscopic examination and the histologic examination. A broad no man's land lies between the ophthalmoscopist and the histologist. This can be bridged by the employment of two methods: first, a slit lamp examination of the removed posterior section of the eyeball and, second, the excision of selected portions of the retina with a 3 or 4 mm. trephine. The isolated retina, without its pigmented epithelium, is seen by transillumination and examined by miscroscope. The tissue may or may not be stained, after the method of Friedenwald, Dunn and others. When this method of examination is exhausted, the disks of retinal tissue are passed through the usual stages of embedding in paraffin, and serial sections are cut and further studied. The observations of the three methods are then correlated.

The article is illustrated.

W. ZENTMAYER.

TESTING NIGHT VISION. N. B. HARMAN, Brit. M. J. **2:** 347 (Sept. 6) 1941.

Further investigations on a previously reported method of testing night vision convinced the author of its value, and he now describes the method again and gives the results of tests on 700 subjects. The apparatus consists of a standard candle, one burning 120 grains (8 Gm.) in an hour, arranged in a box so that a beam of light radiates in one direction only. The test objects are white disks mounted on black velvet and hung at a distance of 5 meters from the candle box. Each disk measures ½ inch (1.3 cm.) in diameter and is separated from other disks by ⅛ inch (0.3 cm.). The disks are grouped in similar patterns, but the number in each group varies. There are four groups of disks numbering from four to seven, and as the baseboard can be hung from any corner there are sixteen possible variations.

The subject's day vision is first tested, and if it is found normal he is tested for night vision in a completely darkened room; fifteen minutes is allowed for dark adaptation.

The subjects were divided into the following groups according to age: group I, 10 to 18; group II, 19 to 40, and group III, 41 and over. Vision in the dark seems to diminish as one grows older.

The author believes that a normal-sighted person at 5 meters should be able to pass the test; persons who require a 4 meter range can be regarded as safe at night; those with a range of 3 meters or less had better stay indoors. Safety in the dark demands an ability to see the disks at not less than 4 meters, and night fliers should have a range of at least 6 meters. The extended trial shows that the method can be used in testing large numbers of people with comparative ease and with exactness.

ARNOLD KNAPP.

Neurology

A CASE OF TUBEROUS SCLEROSIS WITH "PHAKOMATA." J. P. MARTIN and L. H. SAVIN, Brit. J. Ophth. **25:** 305 (July) 1941.

A man aged 34 years had been mentally deficient and had had epileptic fits since early childhood. Attendants noticed that his vision was failing. The face exhibited typical adenoma sebaceum, and elsewhere on the body there were neurofibromas. His mentality was of a low order, and there were features suggestive of dementia praecox.

The vision was probably light perception. The right optic disk was swollen and gray. Near the macula there was a grayish mottled swelling with an elevation of 0.5 D. and a diameter of ½ disk diameter. Several raised white patches were also present on the retina. The left disk was swollen and elevated 2 D. and contained a small white tumor, more or less globular and slightly pedunculated. Its surface was mulberry-like and glistened as though composed of numerous minute crystals. About 1 disk diameter from the edge of the disk there was a white elongated swelling measuring 2 by 1 disk diameter. The surface was smooth and was elevated 3 D.

The phakomata of the left disk was presumably the manifestation of tuberous sclerosis of the nerve head.

One colored and one black and white illustration accompany the article.

W. ZENTMAYER.

REPORT OF A CASE OF WERNICKE'S SYNDROME COMPLICATING PREGNANCY AND ASSOCIATED WITH OCULAR COMPLICATIONS. G. BLACK, Brit. J. Ophth. **25:** 424 (Sept.) 1941.

When three months pregnant the patient began to have severe headaches accompanied by vomiting and lasting for several hours. About six weeks later failure of vision, two or three deeply placed retinal hemorrhages in the right eye and several large retinal hemorrhages about the disk in the left eye were noted. The vision in each eye was reduced to perception of hand movements. The patient was drowsy. There were no ocular palsies. The blood pressure was normal, and the urine was "clear." The possibility of toxemia of pregnancy was considered; however, on account of the existence of cerebral signs it was decided before terminating the pregnancy to administer intensive doses of vitamin B complex. The effect was dramatic. The vision was immediately improved, and in four hours the patient was able to tell time on the ward clock. As there was no evident change in the condition of the fundi, the visual impairment was supposed to be due in part to

a toxic or nutritional effect on the neural elements. The patient went on to complete recovery of vision, with slight pallor of the right disk. An uncomplicated labor followed.

The author thinks that the condition sufficiently resembled the published accounts of Wernicke's disease to be regarded as such, and if it was Wernicke's disease the case supports the view that this is due in part at least to a deficiency of vitamin B. W. ZENTMAYER.

Parasites

SUBRETINAL CYSTICERCUS. A. URRETS ZAVALIA and M. H. DE ANQUIN, Arch. de oftal. de Buenos Aires **15:** 47 (Feb.) 1940.

A case is reported with the ophthalmoscopic observations illustrated by a stereoscopic photograph, three retinographs and a colored drawing. The patient was an Argentine farm boy aged 18. The parasite was situated in the macular region. The eye was treated with radium (20 mg. filtered through a plate for forty-eight hours), the treatment being followed first by a reduction and finally by an abolition of mobility. Eventually the lesion was reduced in size, with opacification of the cyst wall, which assumed a yellowish red coloration. There was a detachment of the surrounding retina with floating opacities in the vitreous.

The paper concludes with a consideration of the general and local findings in retinal cysticercosis. C. E. FINLAY.

Refraction and Accommodation

WHAT SUBLUXATED LENSES REVEAL ABOUT THE MECHANISM OF ACCOMMODATION. W. H. LUEDDE, Am. J. Ophth. **24:** 40 (Jan.) 1941.

Luedde cites cases of subluxation of the lens which tend to discredit the Helmholtz theory of accommodation. He reports 1 case of subluxation of the lens from a football injury in which vision was normal with glasses and there was a considerable range of accommodation. There was iridodonesis for distant but not for near vision. There was no sign of relaxation until the maximum of the accommodation for the involved eye (+ 4 D.) was reached. W. S. REESE.

Retina and Optic Nerve

RETINOPATHIA CENTRALIS ANGIOSPASTICA (ANGIONEUROTICA), AND SEROSA ALLERGICA, AND THEIR RELATION TO DETACHMENT OF THE RETINA. A. LOEWENSTEIN, Brit. J. Ophth. **25:** 369 (Aug.) 1941.

Loewenstein gives the following summary of the several cases recorded in the article:

"One case of a central retinal process is understood to be an angioneurotic retinopathy of unknown, probably allergic, origin. A second case with exophthalmos and limitation of eye movements with sub- or

intra-macular exudate is diagnosed as posterior scleritis with exudation both into the orbital tissues and sub-retinally. A third case shows a central fundus picture analogous to the second one in connection with a typical tuberculous iridocyclitis. A fourth shows a chemotic sub-conjunctival bleb with, later on, corresponding retinal detachment in a myopic eye. The author emphasizes the fact that the allergic inflammatory reaction—tuberculous or non-tuberculous—is always characterised by a primary narrowing of the smallest vessels with an oedematous imbibition of the surrounding tissue. The allergic spasm of the retinal and choroidal vessels plays a dominant part in the development of the central retinopathy. Specific processes in the choroid and sclera with exudation cause retinal detachment. In the myopic or senile retina, the occurrence of exudate in the presence of cystic degeneration may easily lead to the production of a tear in the retina and a detachment of progressive character."

W. ZENTMAYER.

SPECIAL CASE OF MELANOSIS FUNDI: BILATERAL CONGENITAL GROUP PIGMENTATION OF THE CENTRAL AREA. A. LOEWENSTEIN and J. STEEL, Brit. J. Ophth. **25:** 417 (Sept.) 1941.

The authors describe first the atypical congenital pigmentation of the retina in which the grouped patches of pigment occupy a sector of the fundus. About 40 cases have been reported. All are similar, and all have the common feature that the central area is always free. A case of group pigmentation is described which according to the authors differs from all others published. The ophthalmoscopic picture was that of seemingly congenital pigment patches located at the central area, symmetric in both eyes, the patches being almost similar in shape and size and surrounded by a halo without reflex, dark by indirect illumination and grayish white by direct illumination. Some of the patches contained grayish white corpuscles, perhaps cysts.

The idea of an atavistic patchlike growth of Sattler's choroidal tapetum layer is mentioned, but it seems not impossible that the patches are provoked by nevus cell groups.

The article is illustrated.

W. ZENTMAYER.

PRIMARY RETINAL INFILTRATION OF PALE, PULVERULENT, STELLATE AND PURPURIC CHARACTER AND ACCOMPANYING NEPHRITIS IS A PATHOGNOMIC SIGN OF AZOTEMIC ANAEMIA. H. LAGRANGE, Brit. J. Ophth. **25:** 443 (Sept.) 1941.

Lagrange says: "There seems to be no question that close relations exist between azotemia and the anaemia accompanying nephritis. This form of anaemia has its own characters and its course is progressive and parallel with the degree in which nitrogenous wastes are retained. Just as pale, pulverulent, stellate and purpuric infiltration of the retina may sometimes be an early sign of pernicious anaemia or myeloid leukaemia, this same form of retinal infiltration may show the coexistence of anaemia and azotemia; and such retinal infiltration may show the malignity of these types of anaemia before the clinical and haematological signs are fully evident. . . .

. . . *"Exudative, pale, pulverulent and purpuric infiltration of the retina is but one of the lesions usually accompanying any grave form of anaemia, azotemic anaemia being no exception to this particular rule.*

"Together with determination of the blood urea, *haematological examination,* including the red cell, white cell and platelet counts, the differential leukocyte count, search for abnormal cell-forms and examination of the type of coagulation present, *supplies information concerning the nature of lesions whose aetiological interpretation may be doubtful."*

W. ZENTMAYER.

HEREDITARY OPTIC ATROPHY WITH DOMINANT TRANSMISSION AND EARLY ONSET. J. G. SCOTT, Brit. J. Ophth. **25:** 461 (Oct.) 1941.

Scott reports on two families, totaling two hundred and fifty members, presenting 61 cases of atrophy of the optic nerve. He makes the following points based on his study of these 61 cases.

"(1) The inheritance is direct from affected male or female.

"(2) 32 males and 29 females are affected.

"(3) Onset is at about three years of age.

"(4) Onset is gradual and unnoticed. Colour vision is not lost early. There is no subsequent deterioration or improvement of visual acuity.

"(5) The base of the 'hill of vision' is normal, but the peak is lost.

"(6) The disk is white, edges clear cut, deep cup.

"The remainder of the fundus is normal, bar the absence of the normal light reflex at the macula."

The article contains a number of illustrations and tables.

W. ZENTMAYER.

ABNORMAL VASCULAR ASPECT IN A CASE OF ARTERIOLAR SPASM. BAILLIART, ROLLIN and PÁTERAKIS, Bull. Soc. d'opht. de Paris **50:** 94 (Feb.) 1939.

A woman 25 years of age noticed a thin black veil which obscured the vision in the lower portion of the visual field of her left eye for ten minutes at a time. This phenomenon occurred almost every day, at no fixed time, and sometimes it occurred as often as two or three times a day. Complete ocular examination, including a study of the visual fields, gave negative results except for the changes in the fundus. There was edema of the disk, which was slight in the temporal sector and was especially visible in the superior, nasal and inferior sectors. The superior temporal vein was so turgescent that it appeared as though there was an aneurysmal communication with the artery. Nevertheless, the venous pressure was unusual in this trunk, which like the other venous branches of the disk presented a spontaneous pulsation. The tonometric measurement of 65/30 showed an arterial pulsation which extended considerably beyond the disk to a distance of 2 to 3 disk diameters. General examination revealed a degree of hyperthyroidism without trembling or tachycardia. The general arterial tension was 130 systolic and 70 diastolic.

L. L. MAYER.

INSTABILITY OF ARTERIAL RETINAL TENSION ORIGINATING IN THE CAROTID SINUS. A. ROLLIN, Bull. Soc. d'opht. de Paris **51:** 10 (Jan.) 1939.

A patient 68 years of age consulted the author because of a subconjunctival hemorrhage. Because general hypertension was suspected, the fundi were examined. In each eye the arterial tree was normal, but the central retinal vein showed a pulsation of 110 per minute. There was some slight edema of the edges of the disk and the macular region. The retinal arterial tension was low. Intraocular tension was normal. The heart was normal, but the blood pressure was 175 systolic and 100 diastolic. As the results of all other examinations were negative, Rollin was disturbed to find such a marked discord in the relation of general arterial tension and that of the retinal artery. Change of body position caused a marked variation in retinal arterial tension. Biomicroscopic study of the conjunctival veins revealed marked fluctuations in caliber on change of position. Rollin concluded that the sympathetic control of the carotid sinus was at fault.

L. L. MAYER.

CLINICAL SIGNS AND ANATOMIC CHANGES IN ALBUMINURIC RETINITIS W. KYRIELEIS, Arch. f. Ophth. **140:** 193 (April) 1939.

One hundred cases of albuminuric retinitis in which there was no pronounced arteriosclerotic or diabetic component were studied. In 50 cases the underlying renal disease was malignant nephrosclerosis. While the most severe forms of retinitis occur in cases in which the renal function is markedly impaired, there is no definite parallelism between renal and ocular findings. The author stresses the significance of narrowing of the entire retinal arterial tree. He considers an arterial caliber of less than two thirds of the caliber of the accompanying vein as definitely pathologic. In 96 of his cases the narrowing of the arterial tree was pronounced; in about 50 it was very severe. There is no simple relation between arterial narrowing in the retina and general blood pressure. In addition to the general arterial constriction, there are localized and transitory constrictions. Visible changes (thickening) of the vessel wall develop and progress at the same rate as the retinitic changes. Kyrieleis describes (pictures) an inverted phenomenon of Gunn, namely, nicking of the vein by an underlying artery. Guist's sign, viz., abnormal width and tortuosity of the small macular vessels, is not a characteristic feature of hypertensive disease but occurs in the severer forms of retinitis and probably indicates peculiar circulatory conditions which belong to the picture or, rather, are the basis of retinitis and not of hypertension. The degree of filling of the retinal capillaries can be estimated on the disk. In 14 cases the disk was pale; in 64, it had normal color, and in 22, it was hyperemic. Capillary hyperemia is usually coupled with severe retinitis. While the retinal arteries appear narrow, there may be no ischemia in the capillaries. The etiologic significance of a circulatory disorder in retinitis cannot be denied, but this disorder is not on the order of ischemia but of the type of "peristatic" hyperemia (Ricker). The lipoid deposits in the outer molecular layer are precipitated foodstuff.

There is no parallelism between the degree of hypertension and the severity of the retinitis. The hypertension as well as the retinitis accompanies or is the result of characteristic alterations in vessel caliber, viz., arterial constriction and, later, capillary atonic dilatation.

The retinitis has a predilection for the posterior pole because of the greater thickness and vascularity of the retina in this region. Azotemia was absent in 60 cases of marked retinitis and therefore was of no causal significance. Kyrieleis refutes Koyanagi's theory of a physiologic secretory function of the pigment epithelium. In retinitis there is no topographic relation between alterations in the pigment epithelium and retinitic lesions.

Despite arterial constriction, the nutritional demands of the tissues can be met by acceleration of the blood stream. If this compensatory mechanism fails because of relaxation and dilatation of the capillary bed, the "peristatic" condition develops which is the basis of retinitis.

P. C. KRONFELD.

Trachoma

THE QUESTION OF THE RICKETTSIAL NATURE OF TRACHOMA. I. A. BENGTSON, Am. J. Ophth. **23:** 770 (July) 1940.

Bengtson reviews the literature on the role of rickettsias in trachoma and describes her experimental work designed to elucidate the rickettsial nature of trachoma.

W. S. REESE.

THE LOCAL USE OF SULFANILAMIDE IN TRACHOMA. K. W. COSGROVE, Am. J. Ophth. **23:** 911 (Aug.) 1940.

Cosgrove gives the following summary:

"The symptomatic relief of the patient with trachoma on local sulfanilamide is apparently as rapid and complete as that obtained from oral medication.

"In 214 eyes, equal improvement of visual acuity was obtained with both oral and local treatment.

"Small dosages of sulfanilamide supplemented by local application can be used in ambulatory clinics with the same results as are obtained from large dosages of the drug.

"It may be possible to prevent the recurrence of trachoma after sulfanilamide therapy by the continued local use of sulfanilamide. Even if the treatment has to be used for the remainder of the patient's life, there would be no danger to his health."

W. S. REESE.

SULFONAMIDE THERAPY OF TRACHOMA. J. E. SMITH, L. A. JULIANELLE and J. H. GAMET, Am. J. Ophth. **24:** 174 (Feb.) 1941.

Smith, Julianelle and Gamet give the following summary and conclusions of their study:

"1. A study of sulfonamide therapy in trachoma has been undertaken in the manner described above.

"2. Following the administration of sulfanilamide *per os* to 26 patients, the disease in 2 was arrested, 11 were improved, and 13 unchanged at the end of the treatment.

"3. Following neoprontosil [azosulfamide] applied topically as already outlined, a definite improvement was observed in all of nine patients. All were subsequently given some other form of treatment in order to render them asymptomatic.

"4. A review of the correlated literature has been made and the results have been analyzed.

"5. A conservative opinion at the present time would be that sulfonamide compounds cause a disappearance of the nonspecific (that is, subjective) symptoms of trachoma and an improvement of varying degrees in the clinical condition; evidence of their curative capacity remains to be established.

"6. It is the opinion of the present writers that in spite of the improvement, 'recovery' from trachoma is not the rule but the exception.

"7. It, therefore, seems the wiser procedure to supplement sulfonamide treatment with one of the more usual forms of local therapy."

W. S. REESE.

Tumors

AN ORBITAL DERMOID (LINED BY SKIN AND MODIFIED CONJUNCTIVA). P. MCG. MOFFATT, Brit. J. Ophth. **25:** 428 (Sept.) 1941.

A youth aged 19 complained of a swelling of the upper and outer angle of the left orbit. The mass had been there as long as he could remember and recently had increased in size. It was now the size of a cherry and, unattached to the overlying skin, was freely movable. When removed it was found to be a cyst with a thin fibrous wall, and it was lined with epithelium. The growth had extended backward under the orbital margin and had assumed an hourglass shape.

The epidermal portion showed a papillary structure, with hair follicles, sebaceous glands and a few sweat glands. Keratinization was well marked. The contents of the cyst were a porridge-like, sebaceous mass containing hairs and desquamated cells. No nerve fibers were found, but, as no special stain was used, this does not exclude their presence.

The article is illustrated.

W. ZENTMAYER.

A CASE OF VON RECKLINGHAUSEN'S DISEASE WITH DIFFUSE NEUROFIBROMATOSIS OF THE CHOROID. S. ROBSON and W. BLACKWOOD, Brit. J. Ophth. **25:** 431 (Sept.) 1941.

The patient was a boy aged 10 years. For four years the upper lid of the right eye was thickened and pendulous. Wormlike swellings could be felt beneath the skin, extending above the eyebrow. Movable swellings were present on the front of the right side of the neck, on the abdomen in the course of the intercostal nerves, in the left groin and on the front of the left shoulder. There was a large café-au-lait patch on the left buttock, and there were smaller ones on the abdomen and the back. Later innumerable café-au-lait spots covered the back and abdomen.

The right eye showed a large detachment of the retina. The eyeball was removed. Histologic study of biopsy specimens from the head and neck showed neurofibromatosis.

Microscopic examination of the optic nerve, optic disk, retina and sclera showed no particular abnormality. The choroid was generally thickened, with a focal accentuation of the thickening. The central tumor contained well formed adult nerve cells, each with a characteristic nucleus and nucleolus. These cells lay in little groups, and between the groups ran whorls and "bundles," which contained myelinated nerves. The "bundles" had the same histologic character as those of the central tumor. The long ciliary nerves running within the substance of the choroid showed no abnormalities. Myelinated nerve fibers were found within the substance of the "round or ovoid bodies." The ovoid bodies were the result of transverse sections of the neurofibromatous bundles which formed the main mass of the tumor. The tumor was only moderately vascular, the blood vessels being well formed and healthy.

In summary the authors say:

"A case of von Recklinghausen's disease has been described with diffuse neurofibromatosis in the course of the short ciliary nerves.

"The histological appearances were similar to previous cases in the literature, including the presence of 'ovoid or round bodies.'

"It has been possible to demonstrate nerve fibers in the 'ovoid or round bodies' and it is suggested that these 'ovoid bodies' are a normal constituent of a diffuse neurofibromatosis."

The article is illustrated.

W. ZENTMAYER.

METASTASIS OF HYPERNEPHROMA INTO THE CHOROID. A. STCHEGLOVA, Vestnik oftal. **18:** 407, 1941.

A detailed review of the literature, statistical data and five photomicrographs are presented. Two cases are reported. In one, six years before the loss of vision in the right eye the left kidney was removed because of hypernephroma. The right eye on examination showed an intraocular tumor and was enucleated. The histologic examination showed that it was a tumor of the choroid and that the tissue closely resembled adrenal tissue. The tumor was transparent, with coarse connective tissue divisions, a beehive-like structure with transparent cells and fine protoplasm.

The second patient complained of having had poor vision in the right eye for a few weeks. The ophthalmoscopic examination revealed at the temporal-upper quadrant a dark-colored tumor which protruded into the vitreous. The retina was detached below. The enucleated eye showed a tumor of the choroid near the equator. The histologic picture of the tissue was not typical of any type of tumor. Soon after the enucleation the patient died, and at autopsy there was observed primary hypernephroma of the left kidney, with metastases into the right kidney, the adrenals, the lungs and the thyroid.

Tumors of the kidneys are rare, comprising about 1.1 per cent of all malignant tumors, and from 90 to 98 per cent of them are hypernephroma. In typical cases the cells resemble those of the adrenals, are lined up in columns and are rich in blood vessels. Metastases of hypernephroma into the eye have been reported in only a few cases.

O. SITCHEVSKA.

Uvea

A Case of Boeck's Sarcoidosis. E. V. Srinivasan, Brit. J. Ophth. **25:** 493 (Oct.) 1941.

A woman aged 45 was operated on successfully for cataract in the left eye. One month later cyclitis developed; this progressed, and six months later there was added deep keratitis involving the lower third of the cornea.

The iris showed several large, rough and irregular reddish yellow nodules. A hard, nodular, tender mass occupied the upper fornix. There were myxedematous changes in the skin in portions of the body.

Roentgenograms showed diffuse fibrosis of the lung fields, with areas of calcification. No biopsy was done, as favorable progress was made with ultraviolet irradiation.

W. Zentmayer.

Gumma of the Irises. V. Papkova, Vestnik oftal. **18:** 441, 1941.

To 1939 there had been reported in the Russian literature 39 cases of gumma of the iris. A woman aged 30 had a growth at the root of each iris, the base being at the angle of the anterior chamber. The size of the growth (5 to 6 mm.), the caseous degeneration, the atrophic patches on the iris, the positive Wassermann reaction of the blood and the disappearance of the tumor as a result of specific treatment made the diagnosis of gumma indisputable. The interesting features of this case were that the gumma was bilateral, there was no tertiary syphilis in the other organs and deep keratitis which improved under specific treatment was present.

O. Sitchevska.

Vision

Scintillating Scotoma and Other Subjective Visual Phenomena. J. E. Weeks, Am. J. Ophth. **23:** 513 (May) 1940.

After describing symptoms in individual cases and discussing the etiology Weeks presents the following conclusions:

"Scintillating scotoma is due to a cerebral angioneurosis affecting the visual cells temporarily without causing their destruction, a phenomenon allied to the cerebro-angioneurosis that determines attacks of hysterical amaurosis, paralysis of ocular muscles, and the explosive cerebral angioneuroses that determine attacks of epileptiform hysteria and epilepsy.

"The hallucinations occurring in homonymous hemianopia are due to the disturbances of visual cells at the cortical visual center, antedating their destruction by the process that determines the hemianopia. The hallucinations never resemble the visual phenomena of scintillating scotoma."

W. S. Reese.

Visual Tracts and Fields

Selection of the Test Object in Perimetry. O. P. Bourbon, Am. J. Ophth. **23:** 1260 (Nov.) 1940.

Bourbon believes that for accuracy and uniformity peripheral fields should be measured with a stimulus of the minimum size that will give distinct central vision, thus placing all eyes on an equal basis notwith-

standing their varying degrees of nonpathologic loss of central vision. He uses the smallest object of which the patient can detect the shape on the perimeter arm when he is tested with two differentially shaped objects.

W. S. REESE.

Therapeutics

VITAMIN "C" (ASCORBIC ACID)—ITS THERAPEUTIC VALUE IN INFLAMMATORY CONDITIONS OF THE CORNEA. T. K. LYLE and D. W. MCLEAN, Brit. J. Ophth. **25:** 286 (June) 1941.

The authors reach the following conclusions:

"1. In certain corneal conditions—notably ulceration, superficial type of keratitis and chronic corneal opacities—treatment by means of ascorbic acid intravenously is of thereapeutic value. The improvement in most cases is almost dramatic.

"2. In most cases treated, there is no reason to believe that a general vitamin 'C' deficiency exists. It appears, therefore, that the beneficial results are obtained by flooding the bloodstream with excess of ascorbic acid.

"3. Ascorbic acid appears to be of no value in the treatment of iritis. It may even have a detrimental effect in certain instances.

"4. The injections used (ascorbic acid 'Roche' concentrated vitamin 'C' ampoules, 500 mgs. per injection) caused no local or general reaction.

"5. *Dosage*:—We recommend the daily injection of 500 mgs. intravenously until active inflammation of the eye has ceased, preferably followed by ascorbic acid tablets given orally (Tabs. ii t.d.s., each tablet containing 250 mgms.)."

W. ZENTMAYER.

SUBCONJUNCTIVAL IMPLANTATION OF CATGUT AS A NEW THERAPEUTIC FACTOR. B. RADZIKHOVSKY, Vestnik oftal **18:** 394, 1941.

Implanted catgut acts similarly to implanted conserved tissue, with the advantage that the method of its application is simple and that it is accessible for use at any time. Catgut no. 4 was implanted into the conjunctiva above the limbus in 14 patients with trachomatous pannus, in 3 with herpetic keratitis and in 3 with scrofulous keratoconjunctivitis. The time of observation was from nine to eighteen months. In 8 cases of trachoma in the cicatricial stage a complete recovery was obtained. The pannus disappeared and there was an improvement of the process in 2 cases. In 4 cases of severe involvement there was no improvement either in the cornea or in the conjunctiva. In the cases of herpetic keratitis the catgut was implanted in ten to sixteen days after the beginning of the disease, after routine measures failed to bring relief. In about a week the inflammatory symptoms disappeared and clearing of the cornea was observed. No favorable results were obtained in the treatment of scrofulous keratoconjunctivitis. In 2 cases an infection occurred at the place of implantation and the catgut had to be removed.

O. SITCHEVSKA.

Society Transactions

EDITED BY DR. W. L. BENEDICT

DETROIT OPHTHALMOLOGICAL SOCIETY

RALPH H. PINO, M.D., *President*

EDMOND L. COOPER, M.D., *Recorder*

December 3, 1941

Recent Advances in Ophthalmic Therapeutics. DR. SANFORD R. GIFFORD (by invitation), Chicago.

The theory of the chemical mediation of nerve impulses has clarified the knowledge of miotic and cycloplegic agents, and research in this field has added several new agents which are of value in ophthalmic therapeutics. Drugs may be classified as parasympathomimetic when their effect is the same as that of stimulation of the parasympathetic nervous system and as sympathomimetic when their effect is the same as that of stimulation of the sympathetic nervous system.

Stimulation of the parasympathetic nervous system causes production of acetylcholine in the ganglions and at the nerve endings in muscle or gland. This substance is constantly being destroyed by cholinesterase. Drugs which affect the parasympathetic nervous system and which act directly on myoneural function include choline, acetylcholine, mecholyl, carbaminoylcholine chloride (doryl), pilocarpine, histamine and furfuryl trimethyl ammonium iodide. Physostigmine and prostigmine acetate act on myoneural function by destroying cholinesterase at the myoneural junctions. The derivatives of choline are unstable and brief in their effect, the most stable of them being carbaminoylcholine chloride.

Stimulation of the sympathetic nervous system results in production of epinephrine at the myoneural junctions. It acts on a preformed substance called presympathin E in muscles which are stimulated to contract and on a preformed substance called presympathin I in muscles which are inhibited by the sympathetic nervous system. Agents which cause the direct formation of sympathin are epinephrine and its derivatives, neosynephrin, benzedrine and paradrine. Cocaine, eucatropine and thyroxin act by sensitizing the muscle cells to the action of sympathin. The action of the group of drugs containing atropine is effective in protecting the myoneural junctions from choline. The effect of choline paralyzes muscles innervated by the parasympathetic nervous system.

When present in effective concentrations in the blood stream and tissues, sulfanilamide and its derivatives have a bacteriostatic effect on certain bacteria. Adequate treatment of infection by these drugs demands that an effective concentration in the blood be maintained until the body's defenses can cope with the infection. Hence a large initial dose is necessary (60 to 80 grains [4 to 5 Gm.] for an adult suffering from a severe infection), and subsequent doses should be frequent and should be

given day and night for several days or until the infection is controlled. The effect of all these drugs is due to the sulfanilamide radical, and four of the group probably have all the qualities attributed to the rest of the group. Sulfanilamide, sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine) and sulfadiazine (2-[paraaminobenzenesulfonamido]-pyrimidine) are fairly diffusible and when given orally reach the ocular media in effective concentrations. Sulfathiazole (2-paraaminobenzenesulfonamido]-thiazole) is much less diffusible than these in the spinal fluid and ocular media. Streptococcic infections respond best to sulfanilamide, pneumococcic infections to sulfapyridine and staphylococcic infections to sulfathiazole. All three organisms respond to sulfadiazine, which produces relatively little toxic effect. Gonococcic and meningococcic infections respond best to sulfapyridine and sulfathiazole.

Aside from keratomalacia and hemeralopia, caused by a definite deficiency of vitamin A, other ocular conditions, such as recurrent sicca and the mild form of epithelial dystrophy (Fuchs), may possibly result from subclinical deficiencies of this vitamin.

The deficiency of vitamin B_1 (thiamine hydrochloride), which causes toxic amblyopia, is most important to ophthalmologists. Thiamine hydrochloride is best administered orally in divided doses, and there is probably no advantage in giving more than 25 mg. a day.

Rosacea keratitis is the only known ocular condition due to a deficency of vitamin B_2 (riboflavin). It may or may not be associated with rosacea lesions of the skin and with cheilosis. The most effective treatment of this condition consists of the intravenous injection of 1 to 2 mg. of riboflavin daily for ten days, followed by the daily oral administration of 5 mg. of the drug together with fairly large doses of the vitamin B complex.

The question of vitamin deficiency in cases of recurrent retinal hemorrhage is to be considered when the condition is not due to hypertension. If tests reveal marked capillary fragility, vitamin P (citrin) is indicated and may be given in daily oral doses of 50 mg. Vitamin C (ascorbic acid) and the vitamin B complex may be of value, but their effectiveness is doubtful. Vitamin K is indicated only when the prothrombin clotting time is prolonged, as it is chiefly in cases of obstructive jaundice and in the newborn.

January 22, 1942

Supranuclear Lesions as They Affect Ocular Movements. Dr. Frank B. Walsh (by invitation), Baltimore

It is well known that stimulation of the cortex in certain areas of the frontal lobes of the brain results in conjugate deviation of the eyes to the contralateral side. Such stimulation applied to the upper parts of these areas results in conjugate deviation downward and to the contralateral side, while stimulation in the lower parts results in conjugate deviation associated with upward movements to the contralateral side. These so-called frontal oculogyric centers are thought to control volitional movements of the eyes. Destruction of one such area or its subcortical projection pathway results in a conjugate deviation of the eyes to the side of the lesion when the lesion is in the hemisphere and in an inability to move the eyes voluntarily to the contralateral side.

Stimulation of certain areas of the cortex of the occipital lobes results in conjugate deviation of the eyes to the opposite side. The occipital oculogyric apparatus controls fixation. The influence exerted by the frontal area on movement of the eyes to stronger movement than that exerted by the occipital area is evidenced by the ocular movements if appropriate stimulations are applied.

These two oculogyric centers are spoken of as primary centers. Subcortical projection pathways pass from them to intermediary supranuclear centers of the opposite side. From these, impulses are brought to bear on the nuclei of the oculomotor nerves (the third, fourth and sixth cranial nerves). The subcortical projection pathway from the frontal area is thought to pass through the internal capsule. The intermediary center for lateral movement is thought to be situated in the region of the nucleus of the abducens nerve. Other such centers may exist in the angular gyrus and in the supramarginal gyrus. Pathways from the occipital centers pass forward to reach the superior colliculus, from whence they make connections with the posterior longitudinal bundle. This bundle is the final mediator of impulses to the oculomotor nuclei.

When volitional control is suspended as a result of a destructive lesion, the optic fixation reflexes account for tonic fixations. The supranuclear origin of the lesion can be demonstrated by obtaining rotation of the eyes through various maneuvers. Some of these are as follows: 1. There may be ability to follow a slowly moving test object. 2. The eyes may be momentarily deviated by quickly rotating the head. Presumably this supplies a stimulus from the semicircular canals. 3. Caloric stimulation (irrigation of the ear with cold water) produces deviation to the side of the irrigation (it is to the opposite side if hot water is used). 4. The presence of Bell's phenomenon in paralysis of volitional upward movement proves the supranuclear origin of the defect. Supranuclear lesions in the midbrain result in deviations which are in the opposite direction to those which originate in the hemisphere, because the subcortical pathways become crossed toward their termination. Pontile supranuclear lesions are frequently accompanied by paralyses which are nuclear in origin.

Vestibular reflexes (which include semicircular canal and otolith reflexes) control ocular fixation while the head is in motion. This has been clearly demonstrated in patients who have had one or both vestibular nerves sectioned for Ménière's disease. The semicircular canal reflexes account for momentary deviation of the eyes. Otolith reflexes appear to control ocular fixation through the weight of the otoliths. When there is a supranuclear palsy accounting for inability to raise or lower the eyes, it seems that with appropriate movements of the head the otolith reflexes may provide tonic fixation of the eyes in either an upward or a downward plane. Other ocular reflexes, such as the tonic neck reflexes and the cochlear reflexes, do not require consideration in most clinical cases.

It is particularly important to recognize internuclear palsies. Anterior internuclear palsy is a condition characterized by inability to move one eye internally beyond the midline. The eye usually can be moved inward in the act of converging, which may be performed normally. It can be made to move inward by appropriate caloric stimulation in rare instances.

Anterior internuclear palsy may be bilateral. Posterior internuclear palsy consists of an inability to abduct one eye. The eye, however, can be abducted by appropriate caloric stimulation.

Recognition of internuclear palsies is extremely important, since they invariably signify a lesion which is situated in, or in the region of, the posterior longitudinal bundle and therefore in the substance of the brain stem.

In the foregoing descriptions only destructive lesions have been mentioned. Irritative lesions of supranuclear origin account for findings directly opposite to those associated with destructive lesions.

(A motion picture was shown which illustrated some lesions of the oculogyric centers and pathways.)

DISCUSSION

Dr. Thomas J. Heldt: In stating what effect supranuclear lesions have on the cerebral integration of ocular movements, Dr. Walsh pertinently emphasized the factor of voluntary fixation and control. He called attention chiefly to destructive lesions. Many implications, hypothetic and otherwise, may be pointed out in consideration of integrations as complex as those which underlie ocular movements. However, cognizance must be taken here of the problem of tonus, as observed in the postural and righting reflexes of Magnus and de Kleyn and in the neck reflexes, when one is turning around on one's own axis, and the matter of *Antriebe,* or impulses of psychomotor and reflex pattern. Certainly vestibular functions and hearing ability, too, are important factors in the cerebral integration of ocular movements, as are those many reflex patterns that find their important wayside stations in the red nucleus.

The condition of the young man shown in the motion picture, who "literally shakes his eyes into position" to utilize their function, suggests to me a strong psychogenic compensatory component. He has become much aware of his trouble, and I wonder whether this awareness is not of greater significance to him than the destructiveness of the lesion from which he suffers. Would Dr. Walsh mention the neurologic diagnosis in this case?

Dr. Frederic Schreiber: Lesions of the oculogyric centers and their subcortical projection pathways are often associated with lesions of other centers and pathways. For instance, a patient with oculogyric crises following encephalitis may be more disturbed by the "thinking spell" that accompanies the rolling up of the eyes than by the abnormal ocular movements themselves. One patient whom I have observed was terrified by the same morbid ideas at the time of each crisis. These spells can be controlled in some cases by destruction of or interference with the oxidation of the cells of the cortex of the frontal lobe.

Klemme, by excising a localized prefrontal cortical area, has abolished oculogyric crises in a patient suffering from Parkinson's disease. Oculogyric crises will be abolished in some cases if the patient will smoke cigarets or cigars containing stramonium. This treatment probably has for its basis the same principle as Dr. Klemme's method. One patient who suffered from oculogyric crises for ten years was so desperate that she threatened suicide. Repeated short anoxic cerebral insults were induced with nitrous oxide anesthesia, which treatment resulted in marked

improvement in her condition. There is, of course, danger of producing too much anoxic destruction of the cerebral cortex with such therapy.

DR. L. J. FOSTER: I should like to inquire whether Dr. Walsh believes that there is any connection between the subcortical projection pathways of the frontal area and those of the occipital area.

DR. FRANK B. WALSH, Baltimore: The boy about whom Dr. Heldt has asked suffered from congenital athetosis.

Dr. Schrieber mentioned the use of nitrous oxide anesthesia in the treatment of oculogyric crises. I have observed a patient in whom nitrous oxide produced extensive cortical lesions. His eyes moved in any direction freely, but he was unable to fix them on objects.

The subcortical pathways from the frontal and the occipital area are undoubtedly integrated. Whether they are connected or not, I do not know.

COLLEGE OF PHYSICIANS OF PHILADELPHIA, SECTION ON OPHTHALMOLOGY

FRANCIS HEED ADLER, M.D., *Chairman*

WARREN S. REESE, M.D., *Clerk*

Dec. 18, 1941

Presentation of a Case. DR. WARREN S. REESE.

The patient was a 25 year old married woman for whom Dr. Reese had been unable to make a definite diagnosis. She was referred by a physician in a neighboring city who had seen her in December 1938, at which time her fundi were normal and her vision could be corrected to normal with relatively weak convex lenses. The following May she complained of gradual loss of vision in both eyes. Examination revealed little change in the fundi since the previous examination. When she was seen by Dr. Reese her vision was 20/200 in each eye without correction. Both disks were pale and their edges were blurred, indicating a previous neuritis or possibly an active low grade inflammation. Each macular region was dark and appeared edematous, and each contained several shiny points and had a degenerative appearance. Throughout each fundi in the region of the posterior pole were a number of grayish white lesions. These were situated beneath the retinal vessels. They were round and had rather blurred edges. The veins were dark and the arteries bright, although in general the vessels seemed fairly normal. The form fields were full, and central scotomas were not found. All systemic and laboratory studies revealed normal findings.

This case had been presented before the New York Ophthalmological Society by Dr. Brittain F. Payne, who informed Dr. Reese that various opinions had been held there concerning the probable diagnosis. In Dr. Reese's estimation the condition simulated either a postinflammatory or a degenerative disease, possibly an abiotrophy, and he was inclined to believe that it came under the latter classification.

DISCUSSION

DR. W. E. FRY: I had an opportunity to examine the patient yesterday afternoon. The fundus picture presents two conspicuous features. The first is that the changes are widespread and appear to be of a diffuse colloid type; the second is that the macular changes if dissociated from the widespread colloid changes remind one very much of those seen in the juvenile type of hereditary macular degeneration.

I have never seen an association of colloid degeneration with this type of macular degeneration before. Whether or not it could occur I do not know. The ophthalmoscopic picture in my mind represents a disease which is chiefly degenerative in nature and which involves the macula. In addition, colloid changes of the lamina vitrea are present.

DR. WILLIAM ZENTMAYER: I do not understand how macular degeneration with vision reduced to 20/200 could be present without central scotoma. My own impression is that the optic nerve is involved, although I am not on safe ground myself if I consider the condition to be retrobulbar neuritis, since in that case, also, there should be a central scotoma.

I really did not make a thorough enough study of the fundus to pass on the nature of the diffuse changes. I take them to be hyaline in character, which is practically what Dr. Fry suggested.

DR. H. M. LANGDON: I believe that the macular changes probably are the source of the visual decline and that the alterations in the head of the optic nerve are due to an ascending degeneration. I am surprised that with vision of 20/200 a central scotoma has not been found. I must say that I believe a thorough search with the aid of the Bjerrum screen would reveal one.

Bilateral Thrombosis of Calcarine Arteries with Sparing of Macular Vision: Presentation of a Case. DR. P. R. MCDONALD.

Bilateral hemianopia was present and was thought to be caused by thrombosis of both calcarine arteries. The only complaint was complete loss of peripheral vision. With correction the patient was able to read 6/6 with either eye and Jaeger type 1 without difficulty. The neurologic and medical examinations revealed no abnormalities. The patient had first, second and third grade fusion, as shown on the synoptophore, and optokinetic nystagmus in all directions was readily elicited. The cortical representation of vision and the vascular supply to the area striata were discussed.

It was concluded that peripheral vision is not essential for stereopsis or spatial orientation and that optic nystagmus may be elicited even if the field is reduced to about 2½ degrees on each side of the point of fixation. Apparently the performance of the complex visual functions were dependent on macular fixation and certain associated pathways, which were not closely allied with the cortical areas supplying peripheral vision.

DISCUSSION

DR. W. I. LILLIE: This is a rather unusual clinical case. I believe there is no question about the diagnosis. The condition has a vascular

origin, which is indicated by the history of a precipitous onset and two distinct episodes. I am sure that ophthalmologists have all encountered cases of bilateral blindness in which the pupillary reflexes were intact. The condition probably was secondary to a toxic state involving the entire visual cortex. The visual loss usually is transitory. Dr. McDonald's diagnosis could be made accurately by exclusion, because if the anterior and the middle cerebral arteries were involved there would be contralateral motor and sensory disturbances. Dr. McDonald did not discuss the controversial point concerning sparing of the macula and whether there was bilateral macular innervation.

The lantern slide showed the vascular supply of the cerebrum. The upper left hand corner showed the middle cerebral artery, which supplies the lateral surfaces of the frontal, temporal and occipital lobes. In a very small area there was an overlapping of the posterior cerebral artery.

It is known that the macular region is represented in the occipital pole. This was proved in the injury cases of the last World War in which homonymous scotomas resulted when this region was involved. In cases of macular preservation with bilateral thrombosis it is easy to imagine that an anomalous branch from the middle cerebral artery to the pole of the occipital lobe gives added circulation (not unlike a cilioretinal artery). These exceptional cases must have an anatomic explanation for the macular preservation. Lesions of the occipital lobe do not give neurologic manifestations. A patient who complains of headaches or presents any signs of increased intracranial pressure plus homonymous hemianopia and normal neurologic signs could be suffering from a lesion in the occipital lobe.

DR. H. M. LANGDON: I want to congratulate Dr. McDonald and to thank him for presenting this unusual and interesting case. The type of bilateral thrombosis which he has analyzed and diagnosed is most remarkable. It was fortunate that the thrombi did not occur simultaneously, because if they had the findings might have been confusing and Dr. McDonald might have had difficulty in making a correct diagnosis.

DR. F. H. ADLER: I feel that cases of this kind are epic. They are of the type which contributed to progress in ophthalmology as related to knowledge of the physiology of the eye and an understanding of visual field defects.

It will be remembered that around 1910 there was a great discussion between Henschen and Willbrandt and von Monikow. Henschen and Willbrandt believed that there was an exact representation of the retinas in the visual cortex, and von Monikow claimed that there was a diffuse representation of the retinas throughout the whole of the visual cortex. Von Monikow was so sure of his belief that he said more or less boastingly that he wished somebody would come along and shoot a central scotoma out of a brain for him. About four years later, with the advent of World War I, his wish was granted.

During the war there were a great many clearcut injuries to the occipital lobe. Some of the patients lived long enough to be examined and have their visual fields recorded. Some of them subsequently died, and complete sections of the brain were obtained. It was found that a

central scotoma actually could be shot out of a brain if the injury was limited to the extreme posterior tip of the occipital lobe.

The case which Dr. McDonald has presented is indicative of several things. It demonstrates that the optomotor centers for the fixation reflexes are localized not only in the parastriate and the peristriate region, as stated before, but right over the striate area itself. In this patient an area of the posterior pole remains intact, which is represented by a field some 5 degrees in extent laterally, and yet the patient has optokinetic nystagmus both to the left and to the right.

This case is of more than academic interest. For patients who suffer from right homonymous hemianopia in which the dividing line between the seeing and the blind area extends through the fixation point, reading is extremely difficult. On the other hand, patients can read with ease who have left homonymous hemianopia that extends directly through the fixation point. It is assumed that the difference in the reading ability of patients with these two types of homonymous hemianopia is due to the fact that the patient with right homonymous hemianopia must search for the letters as he reads from left to right, whereas the patient with left homonymous hemianopia is using the seeing halves of his fields, so to speak.

There is another reason for the difference between these two types. Reading is accomplished through a series of involuntary movements by which the eyes make five or six jumps across the page of ordinary print. A number of letters are scanned at each jump. These reflex movements of the eyes are brought about by stimuli from the optokinetic centers in the occipital lobe. If a patient has right homonymous hemianopia he gets no stimulus from the blind fields for moving the eyes to the right, and hence there are no reflex movements of the eyes to the right. All movements must be made voluntarily, and this makes for awkward and difficult reading.

The patient whom Dr. McDonald presented could read with ease, a fact which indicates that it takes only a small part of the right visual field to produce reflex movements of fixation. His case demonstrates, therefore, that it takes only about 3 to 5 degrees of the central field to produce the movements of fixation necessary for reading. It was formerly assumed that the reflex movements were produced from the peristriate and the parastriate region, which are well outside the fovea, and no one, as far as I am aware, has shown that the actual reflex could take place from the foveal cortex itself.

DR. P. R. MCDONALD: I should like to thank Drs. Lillie, Langdon and Adler for their discussions. Unfortunately, the visual fields were not obtainable at the time of the first accident, and I presumed that the patient had right homonymous hemianopia. He claimed that he could not see to the right with either eye. The examination was made by Dr. Gardiner, who decided that the patient had homonymous hemianopia, although visual fields were not taken.

I believe that any discussion concerning macular vision is not apropos in this case, as the fields did not prove one thing or the other. Dr. Langdon mentioned that this is the only case of its type to be reported in the literature. This is true of the American literature; several cases of the type have appeared in the foreign literature

Obstacle to Squint Training—Amblyopia. DR. J. B. FELDMAN and ANNABEL F. TAYLOR, R. N.

This article will be published in full in a future issue of the ARCHIVES.

DISCUSSION

DR. P. J. KENNEDY: I enjoyed Dr. Feldman's paper very much. I should like to discuss briefly a few of the things he brought out. First, the refractive error is no index of the degree of amblyopia. Second, the visual acuity varies with the interest of the patient, the methods of examination and the patience of the examiner. These factors are also concerned when one measures the angle of squint.

The question as to whether or not the patients had scotomas can be answered as follows: They had two types of scotomas, absolute and relative. Such patients do not have absolute scotomas if the target is large enough. If the target is small enough, i. e. if a 1 or 3 mm. instead of a 9 or 11 mm. target is used, they have scotomas, and these factors should be taken into consideration in any statistics pertaining to the presence or absence of scotomas in cases of amblyopia.

Incidentally, the absence of constant simultaneous foveal perception could be demonstrated by any ophthalmologist who would take the time to sit down before a synoptophore.

With regard to the development of amblyopia in the cases which Dr. Feldman reported, all the patients were blind at birth, and vision developed later. One sees amblyopia in children as a rule, or if the squint has not become manifest until adult life a record of the normal vision has not been made previous to the time the patient consults an oculist. Therefore, one is justified in assuming that the amblyopia present is due to a lack of development of vision rather than to a development of amblyopia.

Dr. Feldman mentioned the Wollensack-Allscope spectacle. He uses it as one of the means of recording visual acuity, and he finds that in patients whose vision is improved to normal by this telescopic lens, orthoptic training will bring the vision practically up to normal and simultaneous macular perception and fusion will be obtained. In those, on the other hand, whose vision is not improved by the telescopic lens, while orthoptic training is not exactly wasted there is little visual improvement. A third group of patients comes between these two groups. In it there is a degree of improvement by orthoptic training commensurate with the degree of improvement in vision found by use of the telescopic lens in the routine examination.

It would be well for all ophthalmologists to use the Wollensack-Allscope spectacle in routine examinations of amblyopes.

DR. H. M. LANGDON: There is one thing which I had hoped Dr. Feldman would mention but which he did not as far as I can recall, and that is: Was there any relation between the degree of amblyopia and the possibility of obtaining fusion? My own experience has been that if one eye has vision of 5/25 or less it is difficult to get fusion until the vision is improved and the amblyopia lessened. The only way to find out whether the amblyopia can be lessened is to attempt to lessen it. There are patients who probably have had some cerebral injury at birth,

and, regardless of the treatment employed, improvement in their vision is not accomplished. Even continuous occlusion of the better eye would not cause the affected eye to take up its normal function. Amblyopia is undoubtedly a great barrier to obtaining binocular vision if it is of sufficient depth or magnitude.

One thing which Dr. Feldman brought out and which I think should be accentuated is that an amblyopic eye once restored to normal will not remain so. The eye must be observed from time to time for evidence of recurrence. I have in mind the case of a 3 year old child who had definite amblyopia. The father had had convergent squint and a partially amblyopic eye. An older brother had had a similar condition. I managed to test the child's visual acuity and found it to be 5/45, and it increased to 5/6 after long occlusion. By the time the child was 6½ years old there was good fusion and the squint had disappeared. I did not see him for seven months, after which the amblyopia had recurred in spite of the fact that the squint had not increased. The fusion was difficult to distinguish but it could be seen if one used a dim illumination for the good eye to accentuate the image for the poor eye. The vision had decreased to 5/25, and I was unable to bring about any improvement.

Dr. Feldman did not mention the age factor when he discussed the treatment for overcoming amblyopia. I presume that he had discovered, as most of us have, that amblyopia can be overcome much more readily in young children than in older persons. My own experience is that amblyopia is not so amenable to treatment after the age of 12 or 13 years as it is before that age. I would say that probably in 95 per cent of patients under 6 or 7 amblyopia is amenable to persistent treatment. The cooperation of the parents is essential. Many patients do not improve because of improper occlusion, which is due to the fact that the parents do not understand its necessity.

DR. J. B. FELDMAN: I wish to express my gratitude to the discussers of my paper for their elucidation of the various factors which play a part in amblyopia. As Dr. Langdon has pointed out, the younger and more intelligent a child is the better will be the results from amblyopic training if such training is effective.

News and Notes

EDITED BY DR. W. L. BENEDICT

UNIVERSITY NEWS

Howe Lecture.—Marion Hines, Ph.D., associate professor of anatomy, Johns Hopkins University School of Medicine, Baltimore, gave the Howe Lecture on Ophthalmology at Harvard Medical School, Boston, on March 17. His subject was "Recent Contributions to the Localization of Vision Within the Central Nervous System." The lecture is given under the auspices of the Howe Laboratory of Ophthalmology at Harvard.

Book Reviews

Fondo de ojo a la luz de sodio (Luz amarilla). By Justo Lijo Pavía. Price, 18 pesos. Pp. 198, with numerous illustrations. Buenos Aires, Argentina: El Ateneo, 1941.

In the illumination of the eyeground with sodium light the short and ultrashort waves of the spectrum are eliminated and the monochromatic light thus obtained allows observation of the retina in one visual plane. Originated by Kleefeld in 1935, this illumination was tried by several authors, who used a lamp in which sodium was volatilized. There was not, however, a reliable model until the Zeiss-Osram lamp put on the market a few weeks before the war, a lamp in which the filament is covered with a layer of alkaline oxide. When hot, this filament emits a large number of electrons, which ionize the atoms of gas (usually neon) filling the glass tube of the lamp. In the beginning the light is orange-red, but when the lamp gets hot it changes to yellow. As the temperature may reach 270 F. the lamp is surrounded by a double glass tube and a vacuum is made between the walls (Dewar glass).

The model should be carefully used, as it can be destroyed if the resistance is more or less than 1.2 amperes.

According to Serr, the yellow light is particularly useful in cases of turbidity of the media. With clear media the fundus takes a gray color, in which the retinal vessels are apparent and hemorrhages show black. The macula has a darker color, with a small reflection in the center. The yellow light penetrates the pigment epithelium and makes visible the choroidal vessels in the majority of cases. Detachments of the retina are easily seen even at the beginning. The disk appears gray. Edema is, however, less marked than with ordinary light. Lijo Pavía has used the lamp and compared the images with those obtained with the ordinary ophthalmoscope and with red-free light. He studied cases of retinal detachment, degenerative lesions in the macula, hypertensive retinitis, injuries, atrophy of the optic nerve, glaucoma simplex and choroiditis.

The descriptions of the fundus lesions are illustrated with numerous photographs, some of them panoramic. However, the lack of explanatory diagrams in many cases makes the too extensive clinical descriptions difficult for the reader to follow. The condensed findings and comparisons in the last chapter are not clearly drawn, and the author fails to show why yellow light should be considered superior to the red-free or to the yellow-green used formerly with screens. From his description it seems that the sodium light shows some details, while the red-free shows others. Both may be used with advantage in the interpretation of macular changes, nerve fiber lesions and retinal diseases.

MANUEL URIBE TRONCOSO.

Directory of Ophthalmologic Societies *

INTERNATIONAL

International Association for Prevention of Blindness

President: Dr. P. Bailliart, 66 Boulevard Saint-Michel, Paris, 6e, France.
Secretary-General: Prof. M. Van Duyse, Université de Gand, Gand, Prov. Ostflandern, Belgium.
All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6e, France.

International Ophthalmologic Congress

President: Prof. Nordenson, Serafimerlasarettet, Stockholm, Sweden.
Secretary: Dr. Ehlers, Jerbanenegade 41, Copenhagen, Denmark.

International Organization Against Trachoma

President: Dr. A. F. MacCallan, 17 Horseferry Rd., London, England.

Pan-American Congress of Ophthalmology

President: Dr. Harry S. Gradle, 58 E. Washington St., Chicago.
Executive Secretaries: Dr. Conrad Berens, 35 E. 70th St., New York. Dr. M. E. Alvaro, 1511 Consolacao, São Paulo, Brazil.

FOREIGN

All-India Ophthalmological Society

President: Dr. B. K. Narayan Rao, Minto Ophthalmic Hospital, Bangalore.
Secretary: Dr. G. Zachariah, Flitcham, Marshall's Rd., Madras.

British Medical Association, Section on Ophthalmology

President: Dr. W. Clark Souter, 9 Albyn Pl., Aberdeen, Scotland.
Secretary: Dr. Frederick Ridley, 12 Wimpole St., London, W. 1.

Chinese Ophthalmology Society

President: Dr. C. H. Chou, 363 Avenue Haig, Shanghai.
Secretary: Dr. F. S. Tsang, 221 Foochow Rd., Shanghai.

Chinese Ophthalmological Society of Peiping

President: Dr. H. T. Pi, Peiping Union Medical College, Peiping.
Secretary: Dr. C. K. Lin, 180 Hsi-Lo-yen, Chienmeng, Peiping.
Place: Peiping Union Medical College, Peiping. Time: Last Friday of each month.

German Ophthalmological Society

President: Prof. W. Lohlein, Berlin.
Secretary: Prof. E. Engelking, Heidelberg.

Hungarian Ophthalmological Society

President: Prof. I. Iwre, Budapest.
Assistant Secretary: Dr. Stephen de Grósz, University Eye Hospital, Mária-utca 39, Budapest.
All correspondence should be addressed to the Assistant Secretary.

Midland Ophthalmological Society

President: Dr. W. Niccol, 4 College Green, Gloucester, England.
Secretary: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Place: Birmingham and Midland Eye Hospital.

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* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date.

NORTH OF ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. A. MacRae, 6 Jesmond Rd., Newcastle-upon-Tyne, England.
Secretary: Dr. Percival J. Hay, 350 Glossop Rd., Sheffield 10, England.
Place: Manchester, Bradford, Leeds, Newcastle-upon-Tyne, Liverpool and Sheffield, in rotation. Time: October to April.

OPHTHALMOLOGICAL SOCIETY OF AUSTRALIA

President: Dr. A. James Flynn, 135 Macquarie St., Sydney.
Secretary: Dr. D. Williams, 193 Macquarie St., Sydney.

OPHTHALMOLOGICAL SOCIETY OF EGYPT

President: Prof. Dr. Mohammed Mahfouz Bey, Government Hospital, Alexandria.
Secretary: Dr. Mohammed Khalil, 4 Baehler St., Cairo.
All correspondence should be addressed to the secretary, Dr. Mohammed Khalil.

OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM

President: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Secretary: Mr. L. H. Savin, 7 Queen St., London, W. 1, England.

OPHTHALMOLOGY SOCIETY OF BOMBAY

President: Dr. D. D. Sathaye, 127 Girgaum Rd., Bombay 4, India.
Secretary: Dr. H. D. Dastur, Dadar, Bombay 14, India.
Place: H. B. A. Free Ophthalmic Hospital, Parel, Bombay 12. Time: First Friday of every month.

OXFORD OPHTHALMOLOGICAL CONGRESS

Master: Dr. Percival J. Hay, 350 Glossop Rd., Sheffield 10, England.
Secretary-Treasurer: Dr. F. A. Anderson, 12 St. John's Hill, Shrewsbury, England.

PALESTINE OPHTHALMOLOGICAL SOCIETY

President: Dr. Arieh Feigenbaum, Abyssinian St. 15, Jerusalem.
Secretary: Dr. E. Sinai, Tel Aviv.

POLISH OPHTHALMOLOGICAL SOCIETY

President: Dr. W. Kapuściński, 2 Waly Batorego, Poznań.
Secretary: Dr. J. Sobański, Lindley'a 4, Warsaw.
Place: Lindley'a 4, Warsaw.

ROYAL SOCIETY OF MEDICINE, SECTION OF OPHTHALMOLOGY

President: Dr. A. J. Ballantyne, 11 Sandyford Pl., Glasgow, C. 3, Scotland.
Secretary: Dr. C. Dee Shapland, 15 Devonshire Pl., London, W. 1, England.

SÃO PAULO SOCIETY OF OPHTHALMOLOGY

President: Dr. Jacques Tupinambo, 258 Inglezes, São Paulo, Brazil.
Secretary: Dr. Silvio de Almeido Toledo, Enfermaria Santa Luzia, Santa Casa de Misericordia, Cezario Motta St.—112, São Paulo, Brazil.

SOCIEDAD OFTALMOLOGIA DEL LITORAL, ROSARIO (ARGENTINA)

President: Prof. Dr. Carlos Weskamp, Laprida 1159, Rosario.
Secretary: Dr. Juan M. Vila Ortiz, Córdoba 1433, Rosario.
Place: Rosario. Time: Last Saturday of every month, April to November, inclusive.
All correspondence should be addressed to the President.

SOCIEDADE DE OPHTHALMOLOGIA E OTO RHINO-LARYNGOLOGIA DA BAHIA

President: Dr. Theonilo Amorim, Barra Avenida, Bahia, Brazil.
Secretary: Dr. Adroaldo de Alencar, Brazil.
All correspondence should be addressed to the President.

SOCIETÀ OFTALMOLOGICA ITALIANA

President: Prof. Dott. Giuseppe Ovio, Ophthalmological Clinic, University of Rome, Rome.
Secretary: Prof. Dott. Epimaco Leonardi, Via del Gianicolo, 1, Rome.

Société Française d'Ophtalmologie

Secretary: Dr. René Onfray, 6 Avenue de la Motte Picquet, Paris, 7e.

Society of Swedish Ophthalmologists

President: Prof. K. G. Ploman, Stockholm.
Secretary: Dr. K. O. Granström, Södermalmstorg 4 Ill tr., Stockholm, Sö.

Tel Aviv Ophthalmological Society

President: Dr. D. Arieh-Friedman, 96 Allenby St., Tel Aviv, Palestine.
Secretary: Dr. Sadger Max, 9 Bialik St., Tel Aviv, Palestine.

NATIONAL

American Medical Association, Scientific Assembly, Section on Ophthalmology

Chairman: Dr. Lawrence T. Post, 508 N. Grand Blvd., St. Louis, Mo.
Secretary: Dr. Derrick Vail, 441 Vine St., Cincinnati.
Place: Atlantic City. Time: June 8-12, 1942.

American Academy of Ophthalmology and Otolaryngology, Section on Ophthalmology

President: Dr. Ralph I. Lloyd, 14–8th Ave., Brooklyn.
President-Elect: Dr. James A. Babbitt, 1912 Spruce St., Philadelphia.
Executive Secretary-Treasurer: Dr. William P. Wherry, 1500 Medical Arts Bldg., Omaha.
Secretary: Dr. G. L. McCormick, 626 S. Central Ave., Marshfield.

American Ophthalmological Society

President: Dr. Allen Greenwood, 82 Commonwealth Ave., Boston.
Secretary-Treasurer: Dr. Eugene M. Blake, 303 Whitney Ave., New Haven, Conn

Association for Research in Ophthalmology, Inc.

Chairman: Dr. John Evans, 23 Schermerhorn St., Brooklyn.
Secretary-Treasurer: Dr. C. S. O'Brien, University Hospital, Iowa City.

Canadian Medical Association, Section on Ophthalmology

President: Dr. Alexander E. MacDonald, 170 St. George St., Toronto.
Secretary-Treasurer: Dr. L. J. Sebert, 170 St. George St., Toronto.

Canadian Ophthalmological Society

President: Dr. J. Vaillancourt, 46 St. Louis St., Quebec.
Secretary-Treasurer: Dr. Alexander E. MacDonald, 421 Medical Arts Bldg., Toronto.

National Society for the Prevention of Blindness

President: Mr. Mason H. Bigelow, 1790 Broadway, New York.
Secretary: Miss Regina E. Schneider, 1790 Broadway, New York.
Executive Director: Mrs. Eleanor Brown Merrill, 1790 Broadway, New York.

SECTIONAL

Academy of Medicine of Northern New Jersey, Section on Eye, Ear, Nose and Throat

President: Dr. Charles W. Barkhorn, 223 Roseville Ave., Newark.
Secretary: Dr. William F. McKim, 317 Roseville Ave., Newark.
Place: 91 Lincoln Park South, Newark. Time: 8:45 p. m., second Monday of each month, October to May.

Central Wisconsin Society of Ophthalmology and Otolaryngology

President: Dr. D. G. Hugo, 130 Main St., Oshkosh.
Secretary: Dr. G. L. McCormick, 626 S. Central Ave., Marshfield.
Place: Land O'Lakes. Time: June 1942.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. William D. Rowland, 84 Commonwealth Ave., Boston.
Secretary-Treasurer: Dr. Trygve Gundersen, 243 Charles St., Boston.
Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time: 8 p. m., third Tuesday of each month from November to April, inclusive.

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

President: Dr. Ralph A. Fenton, 1020 S. W. Taylor St., Portland, Ore.
Secretary-Treasurer: Dr. C. Allen Dickey, 450 Sutter St., San Francisco.
Place: Portland, Ore. Time: May 11-14, 1942.

PUGET SOUND ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Spencer S. Howe, 103 E. Holly St., Bellingham, Wash.
Secretary-Treasurer: Dr. Barton E. Peden, 419 Stimson Bldg., Seattle.
Place: Seattle or Tacoma, Wash. Time: Third Tuesday of each month, except June, July and August.

ROCK RIVER VALLEY EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. W. H. Elmer, 321 W. State St., Rockford, Ill.
Secretary-Treasurer: Dr. Harry R. Warner, 321 W. State St., Rockford, Ill.
Place: Rockford, Ill., or Janesville or Beloit, Wis. Time: Third Tuesday of each month from October to April, inclusive.

SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. M. Kessler, 311 Center Ave., Bay City, Mich.
Secretary-Treasurer: Dr. J. H. Curts, 330 S. Washington Ave., Saginaw, Mich.
Place: Saginaw or Bay City, Mich. Time: Second Tuesday of each month, except July and August.

SIOUX VALLEY EYE AND EAR ACADEMY

President: Dr. J. C. Davis, 1615 Howard St., Omaha.
Secretary-Treasurer: Dr. J. E. Dvorak, 408 Davidson Bldg., Sioux Falls, S. D.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. L. Chester McHenry, Medical Arts Bldg., Oklahoma City.
Secretary: Dr. J. W. Jervey Jr., 101 Church St., Greenville, S. C.
Place: Richmond, Va. Time: November 1942.

SOUTHWESTERN ACADEMY OF EYE, EAR, NOSE AND THROAT

President: Dr. H. L. Brehmer, 221 W. Central Ave., Albuquerque, N. Mex.
Secretary: Dr. A. E. Cruthirds, 1011 Professional Bldg., Phoenix, Ariz.
Place: Albuquerque, N. Mex. Time: November 1942.

SOUTHWESTERN MICHIGAN TRIOLOGICAL SOCIETY

President: Dr. W. M. Dodge, 716 First National Bank Bldg., Battle Creek.
Secretary-Treasurer: Dr. Kenneth Lowe, 25 W. Michigan Ave., Battle Creek.
Time: Last Thursday of September, October, November, March, April and May.

WESTERN PENNSYLVANIA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. C. H. Bailey, 29 S. Oakland Ave., Sharon.
Secretary-Treasurer: Dr. J. McClure Tyson, Deposit Nat'l Bank Bldg., DuBois.

STATE

ARKANSAS STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. R. R. Kirkpatrick, 6th and Walnut Sts., Texarkana, Ark.
Secretary-Treasurer: Dr. Raymond C. Cook, 701 Main St., Little Rock.

COLORADO OPHTHALMOLOGICAL SOCIETY

President: Dr. William M. Bane, 1612 Tremont Pl., Denver.
Secretary: Dr. Harry Shankel, Republic Bldg., Denver.
Place: University Club, Denver. Time: 7:30 p. m., third Saturday of each month, October to May, inclusive.

Connecticut State Medical Society, Section on Eye, Ear, Nose and Throat

President: Dr. Edward N. DeWitt, 836 Myrtle Ave., Bridgeport.
Secretary-Treasurer: Dr. Henry L. Birge, 179 Allyn St., Hartford.

Eye, Ear, Nose and Throat Club of Georgia

President: Dr. E. N. Maner, 247 Bull St., Savannah.
Secretary-Treasurer: Dr. C. K. McLaughlin, 567 Walnut St., Macon.

Indiana Academy of Ophthalmology and Oto-Laryngology

President: Dr. F. McK. Ruby, Union City.
Secretary: Dr. Edwin W. Dyar Jr., 23 E. Ohio St., Indianapolis.
Place: French Lick. Time: First Wednesday in April.

Iowa Academy of Ophthalmology and Oto-Laryngology

President: Dr. J. K. Von Lackum, 117–3d St. S. E., Cedar Rapids.
Secretary-Treasurer: Dr. B. M. Merkel, 604 Locust St., Des Moines.

Louisiana-Mississippi Ophthalmological and Otolaryngological Society

President: Dr. Henry N. Blum, 912 American Bank Bldg., New Orleans.
Secretary-Treasurer: Dr. Edley H. Jones, 1301 Washington St., Vicksburg, Miss.

Michigan State Medical Society, Section of Ophthalmology and Otolaryngology

Chairman: Dr. Robert H. Fraser, 25 W. Michigan Ave., Battle Creek.
Secretary: Dr. R. G. Laird, 114 Fulton St., Grand Rapids.

Minnesota Academy of Ophthalmology and Otolaryngology

President: Dr. Erling Wilhelm Hansen, 78 S. 9th St., Minneapolis.
Secretary-Treasurer: Dr. George E. McGeary, 920 Medical Arts Bldg., Minneapolis.
Time: Second Friday of each month from October to May.

Montana Academy of Oto-Ophthalmology

President: Dr. William J. Marshall, 335 Owen St., Missoula.
Secretary: Dr. Fritz D. Hurd, 309 Medical Arts Bldg., Great Falls.

Nebraska Academy of Ophthalmology and Otolaryngology

President: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. John Peterson, 1307 N St., Lincoln.

New Jersey State Medical Society, Section on Ophthalmology, Otology and Rhinolaryngology

Chairman: Dr. Edgar P. Cardwell, 47 Central Ave., Newark.
Secretary: Dr. Arthur E. Sherman, 243 S. Harrison St., East Orange.

New York State Medical Society, Eye, Ear, Nose and Throat Section

Chairman: Dr. Searle B. Marlow, 109 S. Warren St., Syracuse.
Secretary: Dr. C. Stewart Nash, 277 Alexander St., Rochester.

North Carolina Eye, Ear, Nose and Throat Society

President: Dr. M. R. Gibson, Professional Bldg., Raleigh.
Secretary: Dr. Vanderbilt F. Couch, 105 W. 4th St., Winston-Salem.

North Dakota Academy of Ophthalmology and Oto-Laryngology

President: Dr. A. E. Spear, Dickinson.
Secretary-Treasurer: Dr. F. L. Wicks, 516–6th St., Valley City.

OREGON ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Paul Bailey, 833 S. W. 11th Ave., Portland.
Secretary-Treasurer: Dr. R. S. Fixott, 1020 S. W. Taylor St., Portland.
Place: Good Samaritan Hospital, Portland. Time: Third Tuesday of each month.

RHODE ISLAND OPHTHALMOLOGICAL AND OTOLOGICAL SOCIETY

Acting President: Dr. N. Darrell Harvey, 112 Waterman St., Providence.
Secretary-Treasurer: Dr. Linley C. Happ, 124 Waterman St., Providence.
Place: Rhode Island Medical Society Library, Providence. Time: 8:30 p. m., second Thursday in October, December, February and April.

SOUTH CAROLINA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. J. L. Sanders, 222 N. Main St., Greenville.
Secretary: Dr. J. H. Stokes, 125 W. Cheves St., Florence.
Place: Columbia. Time: November 1942.

TENNESSEE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Wesley Wilkerson, 700 Church St., Nashville.
Secretary-Treasurer: Dr. W. D. Stinson, 124 Physicians and Surgeons Bldg., Memphis.

TEXAS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. E. L. Goar, 1300 Walker Ave., Houston.
Secretary: Dr. Dan Brannin, 929 Medical Arts Bldg., Dallas.

UTAH OPHTHALMOLOGICAL SOCIETY

President: Dr. Everett B. Muir, Boston Bldg., Salt Lake City.
Secretary-Treasurer: Dr. Earl H. Phillips, 623 Judge Bldg., Salt Lake City.
Place: University Club, Salt Lake City. Time: 7:00 p. m., third Monday of each month.

VIRGINIA SOCIETY OF OTO-LARYNGOLOGY AND OPHTHALMOLOGY

President: Dr. Mortimer H. Williams, 30½ Franklin Rd. S. W., Roanoke.
Secretary-Treasurer: Dr. Meade Edmunds, 34 Franklin St., Petersburg.

WEST VIRGINIA STATE MEDICAL ASSOCIATION, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. George Traugh, 309 Cleveland Ave., Fairmont.
Secretary: Dr. Welch England, 621½ Market St., Parkersburg.

LOCAL

AKRON ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. George E. Ferguson, Second National Bldg., Akron, Ohio.
Secretary-Treasurer: Dr. D. F. Mathias, First Central Tower, Akron, Ohio.
Time: First Monday in January, March, May and November.

ATLANTA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Stacy C. Howell, 144 Ponce de Leon Ave. N. E., Atlanta, Ga.
Secretary: Dr. Lester A. Brown, 478 Peachtree St. N. E., Atlanta, Ga.
Place: Grady Hospital. Time: 6:00 p. m., second Wednesday of each month from October to May.

BALTIMORE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Ernst Bodenheimer, 1212 Eutaw Pl., Baltimore.
Secretary: Dr. Thomas R. O'Rourk, 104 W. Madison St., Baltimore.
Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m. fourth Thursday of each month from October to March.

Birmingham Eye, Ear, Nose and Throat Club

President: Each member, in alphabetical order.
Secretary: Dr. Luther E. Wilson, 919 Woodward Bldg., Birmingham, Ala.
Place: Tutwiler Hotel. Time: 6:30 p. m., second Tuesday of each month, September to May, inclusive.

Brooklyn Ophthalmological Society

President: Dr. Maurice Wieselthier, 1322 Union St., Brooklyn.
Secretary-Treasurer: Dr. Harold F. Schilback, 142 Joralemon St., Brooklyn.
Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

Buffalo Ophthalmologic Club

President: Dr. Meyer H. Riwchun, 367 Linwood Ave., Buffalo.
Secretary-Treasurer: Dr. Sheldon B. Freeman, 196 Linwood Ave., Buffalo.
Time: Second Thursday of each month.

Chattanooga Society of Ophthalmology and Otolaryngology

President: Each member, in alphabetical order.
Secretary: Dr. Douglas Chamberlain, Chattanooga Bank Bldg., Chattanooga, Tenn.
Place: Mountain City Club. Time: Second Thursday of each month from September to May.

Chicago Ophthalmological Society

President: Dr. Sanford Gifford, 720 N. Michigan Ave., Chicago.
Secretary-Treasurer: Dr. Vernon M. Leech, 55 E. Washington St., Chicago.
Place: Chicago Towers Club, 505 N. Michigan Ave. Time: Third Monday of each month from October to May.

Cincinnati General Hospital Ophthalmology Staff

Chairman: Dr. D. T. Vail, 441 Vine St., Cincinnati.
Secretary: Dr. A. A. Levin, 441 Vine St., Cincinnati.
Place: Cincinnati General Hospital. Time: 7:45 p. m., third Friday of each month except June, July and August.

Cleveland Ophthalmological Club

Chairman: Dr. W. J. Abbott, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. L. V. Johnson, 2065 Adelbert Rd., Cleveland.
Time: Second Tuesday in October, December, February and April.

College of Physicians, Philadelphia, Section on Ophthalmology

Chairman: Dr. Francis H. Adler, 313 S. 17th St., Philadelphia.
Clerk: Dr. W. S. Reese, 1901 Walnut St., Philadelphia.
Time: Third Thursday of every month from October to April, inclusive.

Columbus Ophthalmological and Oto-Laryngological Society

Chairman: Dr. C. D. Postle, 240 E. State St., Columbus, Ohio.
Secretary-Treasurer: Dr. Hugh C. Thompson, 289 E. State St., Columbus, Ohio.
Place: The Neil House. Time: 6 p. m., first Monday of each month.

Corpus Christi Eye, Ear, Nose and Throat Society

Chairman: Dr. F. K. Stroud, 416 Chaparral St., Corpus Christi, Texas.
Secretary: Dr. Arthur Padilla, 414 Medical Professional Bldg., Corpus Christi, Texas.
Time: Second Friday of each month from October to May.

Dallas Academy of Ophthalmology and Oto-Laryngology

President: Dr. L. A. Nelson, 4105 Live Oak St., Dallas, Texas.
Secretary: Dr. S. F. Harrington, 921 Medical Arts Bldg., Dallas, Texas.
Place: Dallas Athletic Club. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Des Moines Academy of Ophthalmology and Otolaryngology

President: Dr. H. C. Schmitz, 604 Locust St., Des Moines, Iowa.
Secretary-Treasurer: Dr. Byron M. Merkel, 604 Locust St., Des Moines, Iowa.
Time: 7:45 p. m., third Monday of every month from September to May.

Detroit Ophthalmological Club

Chairman: Members rotate alphabetically.
Secretary: Dr. Harvey E. Dowling, 2414 Eaton Tower, Detroit.
Time: 6:30 p. m., first Wednesday of each month.

Detroit Ophthalmological Society

President: Dr. Parker Heath, 1553 Woodward Ave., Detroit.
Secretary: Dr. Leland F. Carter, 1553 Woodward Ave., Detroit.
Place: Club rooms of Wayne County Medical Society. Time: Third Thursday of each month from November to April, inclusive.

Eastern New York Eye, Ear, Nose and Throat Association

President: Dr. James M. Dunn, 1352 Union St., Schenectady.
Secretary-Treasurer: Dr. Joseph L. Holohan, 330 State St., Albany.
Time: Third Wednesday in October, November, March, April, May and June.

Fort Worth Eye, Ear, Nose and Throat Society

President: Dr. W. R. Thompson, 602 W. 10th St., Fort Worth, Texas.
Secretary-Treasurer: Dr. A. E. Jackson, 602 W. 10th St., Fort Worth, Texas.
Place: Medical Hall, Medical Arts Bldg. Time: 7:30 p. m., first Friday of each month except July and August.

Houston Academy of Medicine, Ophthalmological and Oto-Laryngological Section

President: Dr. Felician J. Slataper, 1110-1111 Medical Arts Bldg., Houston, Texas.
Secretary: Dr. Theo. L. Holland, 611 Medical Arts Bldg., Houston, Texas.
Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., second Thursday of each month from September to June.

Indianapolis Ophthalmological and Otolaryngological Society

President: Dr. John I. Garret, 57 Stokes Bldg., Indianapolis.
Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.
Place: Indianapolis Athletic Club. Time: 6:30 p. m., second Thursday of each month from November to May.

Kansas City Society of Ophthalmology and Oto-Laryngology

President: Dr. Homer Beal, 1103 Grand Ave., Kansas City, Mo.
Secretary: Dr. Desmond Curran, Federal Reserve Bank Bldg., Kansas City, Mo.
Time: Third Thursday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Long Beach Eye, Ear, Nose and Throat Society

Chairman: Dr. Harold Snow, 614 S. Pacific Ave., San Pedro, Calif.
Secretary-Treasurer: Dr. Oliver R. Nees, 508 Times Bldg., Long Beach, Calif.
Place: Professional Bldg. Time: Last Wednesday of each month from October to May.

Los Angeles Society of Ophthalmology and Otolaryngology

President: Dr. John Osburn, 523 W. 6th St., Los Angeles.
Secretary-Treasurer: Dr. Colby Hall, 1136 W. 6th St., Los Angeles.
Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: 6:00 p. m., fourth Monday of each month from September to May, inclusive.

Louisville Eye and Ear Society

President: Dr. Joseph S. Heitger, Heyburn Bldg., Louisville, Ky.
Secretary-Treasurer: Dr. J. W. Fish, 321 W. Broadway, Louisville, Ky.
Place: Brown Hotel. Time: 6:30 p. m., second Thursday of each month from September to May, inclusive.

Lower Anthracite Eye, Ear, Nose and Throat Society

Chairman: Each member in alphabetical order.
Secretary: Dr. James J. Monohan, 31 S. Jardin St., Shenendoah, Pa.

Medical Society of the District of Columbia, Section of Ophthalmology and Otolaryngology

Chairman: Dr. E. J. Cummings, 1835 I St. N. W., Washington.
Secretary: Dr. P. S. Constantinople, 1835 I St. N. W., Washington.
Place: 1718 M St. N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

Memphis Society of Ophthalmology and Otolaryngology

Chairman: Each member, in alphabetical order.
Secretary: Dr. Sam H. Sanders, 1089 Madison Ave., Memphis, Tenn.
Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month from September to May.

Milwaukee Oto-Ophthalmic Society

President: Dr. John W. Truitt, 161 W. Wisconsin Ave., Milwaukee.
Secretary-Treasurer: Dr. Ralph T. Rank, 238 W. Wisconsin Ave., Milwaukee.
Place: University Club. Time: 6:30 p. m., second Tuesday of each month.

Montgomery County Medical Society

Chairman: Dr. H. V. Dutrow, 1040 Fidelity Medical Bldg., Dayton, Ohio.
Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.
Place: Van Cleve Hotel. Time: 6:30 p. m., first Tuesday of each month from October to June, inclusive.

Montreal Ophthalmological Society

President: Dr. J. Rosenbaum, 1396 Ste. Catherine St. W., Montreal, Canada.
Secretary: Dr. L. Tessier, 1230 St. Joseph Blvd. E., Montreal, Canada.
Time: Second Thursday of October, December, February and April.

Nashville Academy of Ophthalmology and Otolaryngology

Chairman: Dr. Andrew Hollabaugh, Doctors Bldg., Nashville, Tenn.
Secretary: Dr. Guy Maness, Medical Arts Bldg., Nashville, Tenn.
Place: St. Thomas Hospital. Time: 8 p. m., third Monday of each month from October to May.

New Haven Ophthalmological Society

President: Dr. William H. Ryder, 185 Church St., New Haven, Conn.
Secretary: Dr. Frederick A. Wies, 255 Bradley St., New Haven, Conn.

New Orleans Ophthalmological and Otolaryngological Society

President: Dr. W. B. Clark, 1012 American Bank Bldg., New Orleans.
Secretary: Dr. Mercer G. Lynch, 1018 Maison Blanche Bldg., New Orleans.
Place: Louisiana State University Medical Bldg. Time: 8 p. m., second Tuesday of each month from October to May.

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman: Dr. Kaufman Schlivek, 1016–5th Ave., New York.
Secretary: Dr. Brittain Payne, 896 Madison Ave., New York.
Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

President: Dr. James W. Smith, 1016–5th Ave., New York.
Secretary: Dr. Benjamin Esterman, 983 Park Ave., New York.
Place: Squibb Hall, 745–5th Ave. Time: 8 p. m., first Monday of each month from October to May, inclusive.

OKLAHOMA CITY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. R. E. Leatherock, Cushing, Okla.
Secretary: Dr. Harry C. Ford, 1014 Medical Arts Bldg., Oklahoma City.
Place: University Hospital. Time: Second Tuesday of each month from September to May.

OMAHA AND COUNCIL BLUFFS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. Harold Gifford, 1620 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m., dinner; 7 p. m., program; third Wednesday of each month from October to May.

PASSAIC-BERGEN OPHTHALMOLOGICAL CLUB

President: Dr. L. Markowitz, 16 Church St., Paterson, N. J.
Secretary-Treasurer: Dr. A. John Reinhorn, 302 Broadway, Paterson, N. J.
Place: Paterson Eye and Ear Infirmary. Time: 9 p. m., last Friday of every month, except June, July and August.

PHILADELPHIA COUNTY MEDICAL SOCIETY, EYE SECTION

Chairman: Dr. Edmund B. Spaeth, 1930 Chestnut St., Philadelphia.
Secretary: Dr. Wilfred E. Fry, 1819 Chestnut St., Philadelphia.
Time: First Thursday of each month from October to May.

PITTSBURGH OPHTHALMOLOGICAL SOCIETY

President: Dr. J. Clyde Markel, 200–9th St., Pittsburgh.
Secretary: Dr. George H. Shuman, 351–5th Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

READING EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Solon L. Rhode, 238 N. 6th St., Reading, Pa.
Secretary: Dr. Paul C. Craig, 232 N. 5th St., Reading, Pa.
Place: Wyomissing Club. Time: 6:30 p. m., third Wednesday of each month from October to July.

RICHMOND OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. W. F. Bryce, Medical Arts Bldg., Richmond, Va.
Secretary: Dr. Richard W. Vaughan, Medical Arts Bldg., Richmond, Va.
Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

ROCHESTER EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. E. J. Avery, 11 N. Goodman St., Rochester, N. Y.
Secretary-Treasurer: Dr. Charles T. Sullivan, 277 Alexander St., Rochester, N. Y.

St. Louis Ophthalmic Society

President: Dr. William M. James, 508 N. Grand Blvd., St. Louis.
Secretary: Dr. H. Rommel Hildreth, 823 Metropolitan Bldg., St. Louis.
Place: Oscar Johnson Institute. Time: Clinical meeting 5:30 p. m., dinner and scientific meeting 6:30 p. m., fourth Friday of each month from October to April, inclusive, except December.

San Antonio Ophthalmo-Oto-Laryngological Society

President: Dr. Dan Russell, 705 E. Houston St., San Antonio, Texas.
Secretary-Treasurer: Dr. P. G. Bowen, 315 Camden St., San Antonio, Texas.
Place: Bexar County Medical Library. Time: 8 p. m., first Tuesday of each month from October to May.

San Francisco County Medical Society, Section on Eye, Ear, Nose and Throat

Chairman: Dr. Fred Boyle, 490 Post St., San Francisco.
Secretary: Dr. Frank Hand, 450 Sutter St., San Francisco.
Place: Society's Bldg., 2180 Washington St., San Francisco. Time: Fourth Tuesday of every month except June, July and December.

Shreveport Eye, Ear, Nose and Throat Society

President: Dr. David C. Swearingen, Slattery Bldg., Shreveport, La.
Secretary-Treasurer: Dr. Kenneth Jones, Medical Arts Bldg., Shreveport, La.
Place: Shreveport Charity Hospital. Time: 7:30 p. m., first Monday of every month except July, August and September.

Spokane Academy of Ophthalmology and Oto-Laryngology

President: Dr. Louis A. Parsell, 407 Riverside Ave., Spokane, Wash.
Secretary: Dr. Robert L. Pohl, 407 Riverside Ave., Spokane, Wash.
Place: Paulsen Medical and Dental Library. Time: 8 p. m., fourth Tuesday of each month except June, July and August.

Syracuse Eye, Ear, Nose and Throat Society

President: Dr. Roy Seeley Moore, 1704 State Tower Bldg., Syracuse, N. Y.
Secretary-Treasurer: Dr. I. H. Blaisdell, 713 E. Genesee St., Syracuse, N. Y.
Place: University Club. Time: First Tuesday of each month except June, July and August.

Toledo Eye, Ear, Nose and Throat Society

Chairman: Dr. John D. Skow, 2001 Collingwood Blvd., Toledo, Ohio.
Secretary: Dr. S. H. Patterson, 125–15th Ave., Toledo, Ohio.
Place: Toledo Club. Time: Each month except June, July and August.

Toronto Academy of Medicine, Section of Ophthalmology

Chairman: Dr. W. R. F. Luke, 316 Medical Arts Bldg., Toronto, Canada.
Secretary: Dr. W. T. Gratton, 216 Medical Arts Bldg., Toronto, Canada.
Place: Academy of Medicine, 13 Queens Park. Time: First Monday of each month, November to April.

Washington, D. C., Ophthalmological Society

President: Dr. E. Leonard Goodman, 1801 I St. N. W., Washington, D. C.
Secretary-Treasurer: Dr. Sterling Bockoven, 1752 Massachusetts Ave. N. W., Washington, D. C.
Place: Episcopal Eye, Ear and Throat Hospital. Time: 7:30 p. m., first Monday in November, January, March and April.

Wilkes-Barre Ophthalmological Society

Chairman: Each member in turn.
Secretary: Dr. Samuel T. Buckman, 70 S. Franklin St., Wilkes-Barre, Pa.
Place: Office of chairman. Time: Last Tuesday of each month from October to May.